"…. Obesity is a chronic, relapsing, neurochemical disease that occurs in genetically susceptible people.

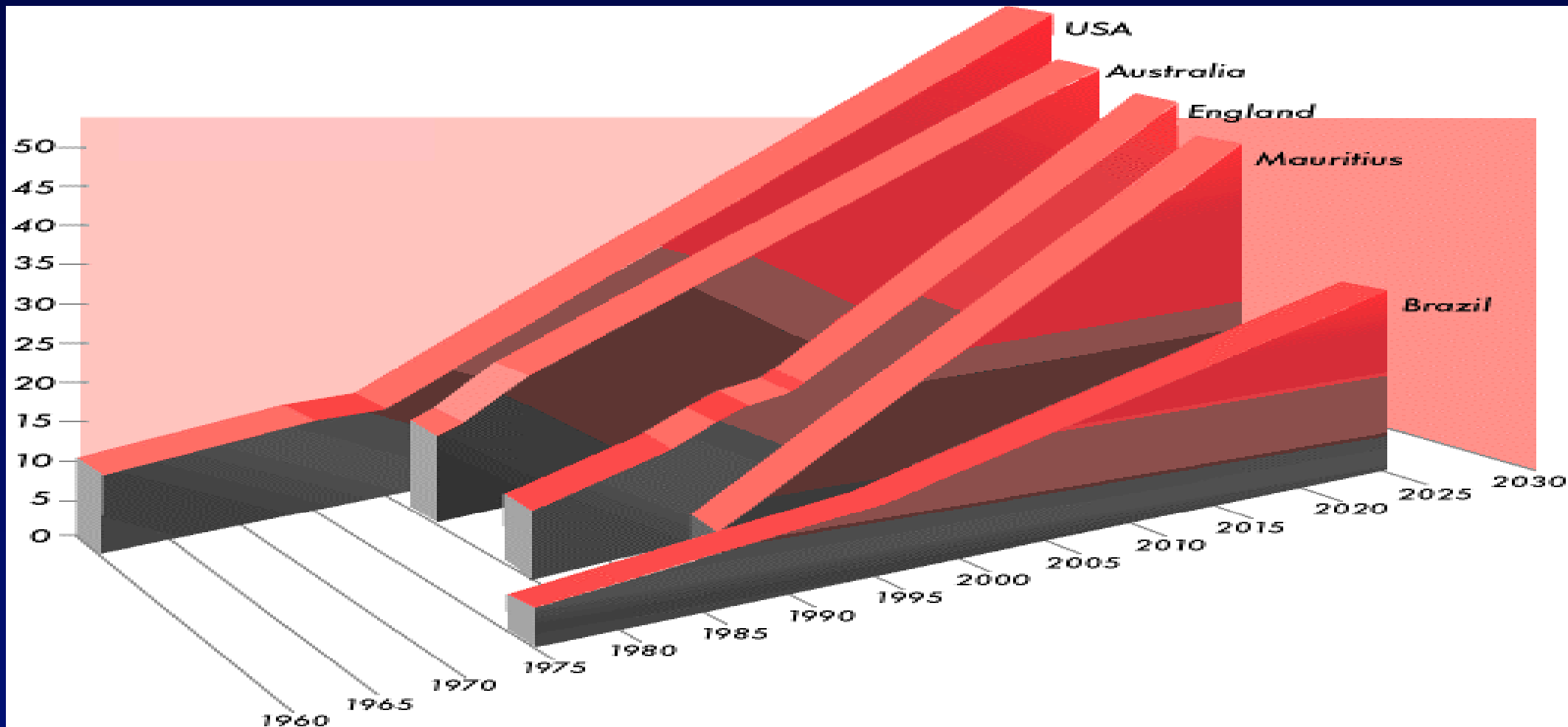
Obesity may be conceptualized as an epidemiological disease with food as an agent that acts on the host to produce disease.

As with most treatments for weight loss, a plateau is reached when the body's neurochemical counter regulatory systems counterbalance the weight loss..."

Current treatment do not cure obesity and thus are only palliative. In particular, diets do not cure obesity.

Bray GA JAMA 2003

La prevalenza di obesità infantile negli USA e in molti paesi del mondo occidentale ha raggiunto **proporzioni epidemiche**: in Canada ad esempio dal 1981 al 1996 è **triplicata**

Mossberg HO. Lancet 1999; 2:491-493

PREVALENCE IN ITALY

	OVERWEIGHT	OBESITY	TOTAL
ADULTS	40%	12%	52%
CHILDREN	24%	12%	36%

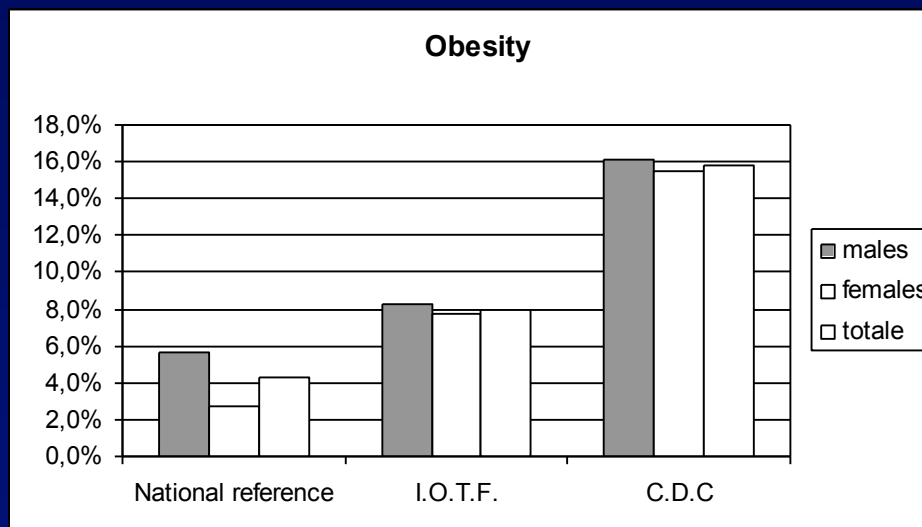
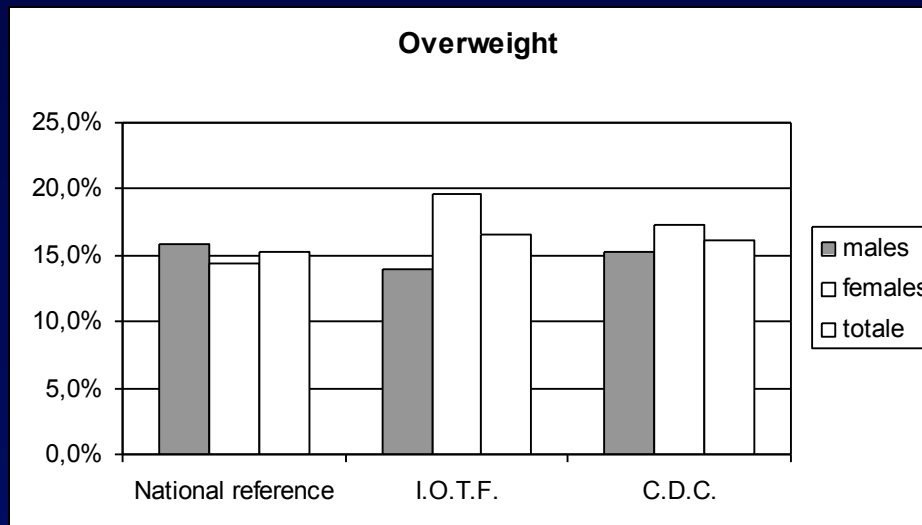
AN OBESE CHILD HAS A 40-80% CHANCES TO MAINTAIN OBESITY IN ADULTHOOD

23% overweight/obese children

49% overweight/obese children

Italian Ministry of Health

PREVALENCE OF OVERWEIGHT AND OBESITY IN 2-6-YEAR-OLD ITALIAN CHILDREN

Maffeis C *et al*. Obes Res, 2006

The Impact of Obesity on Health Service Utilization and Costs in Childhood

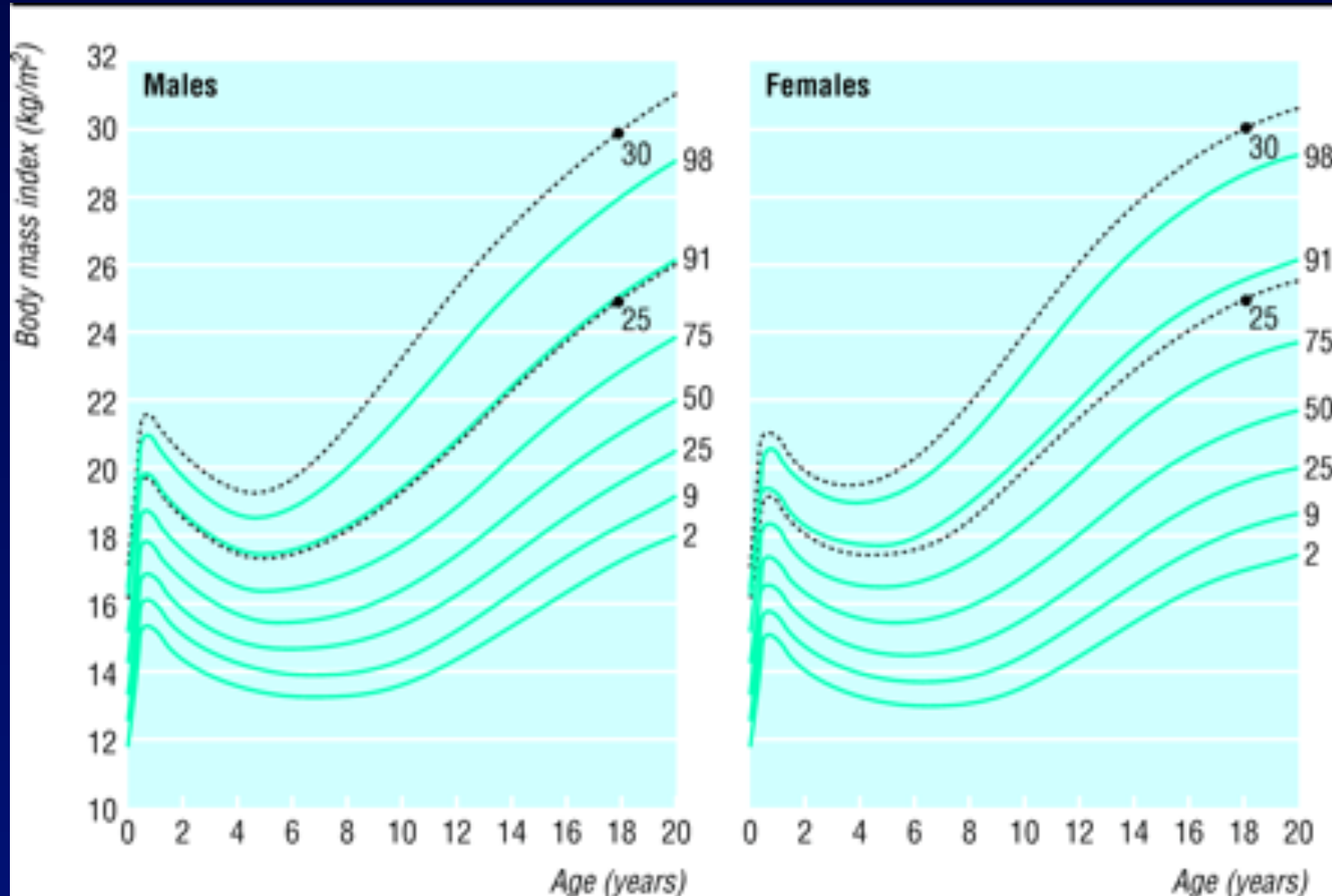
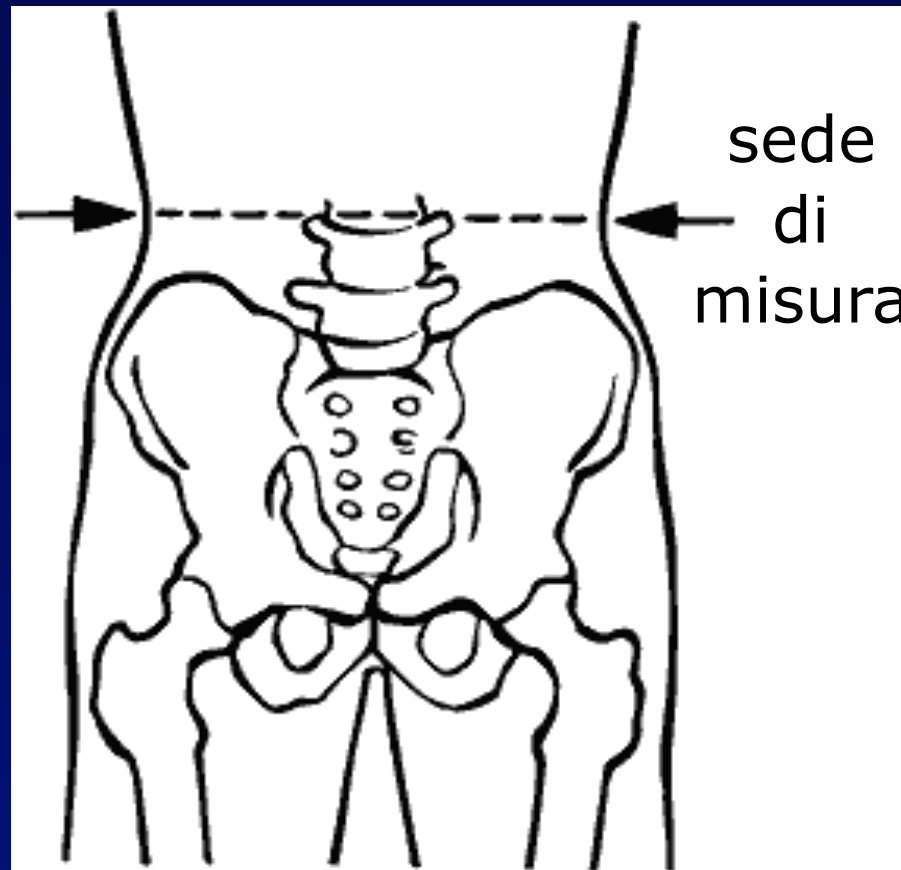
The 2002-5 Medical Expenditure Panel Survey

6 – 19-year-old children and adolescents

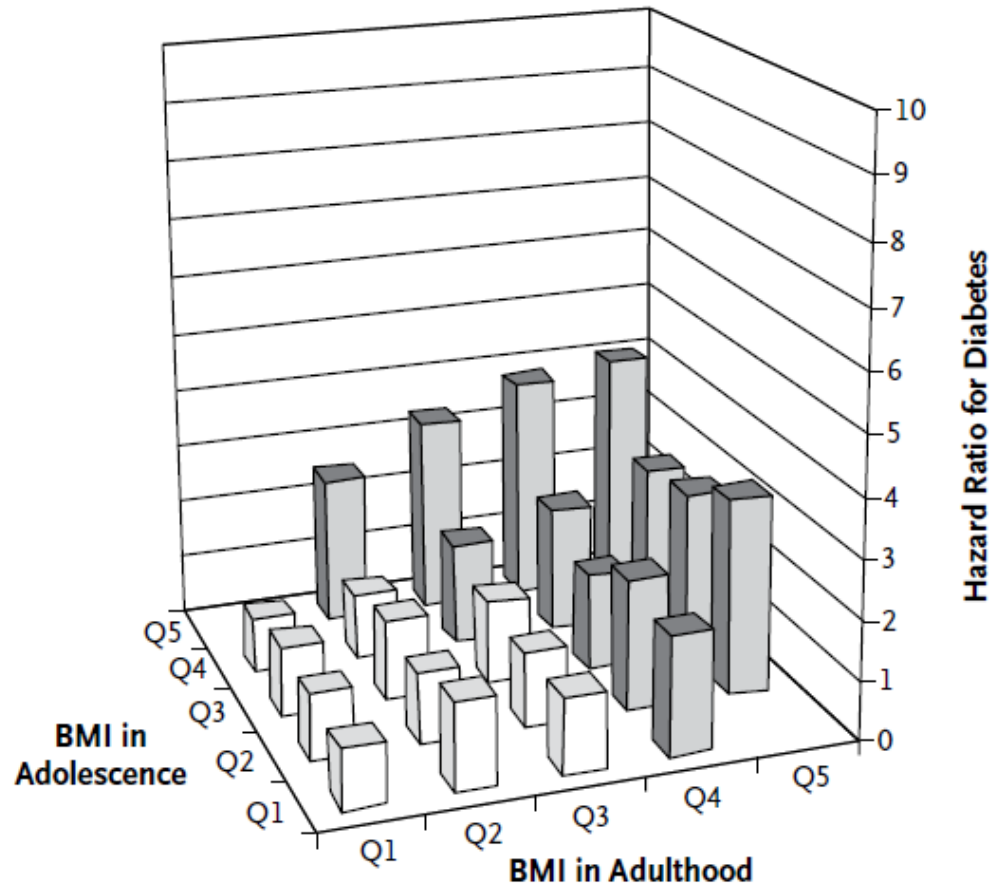
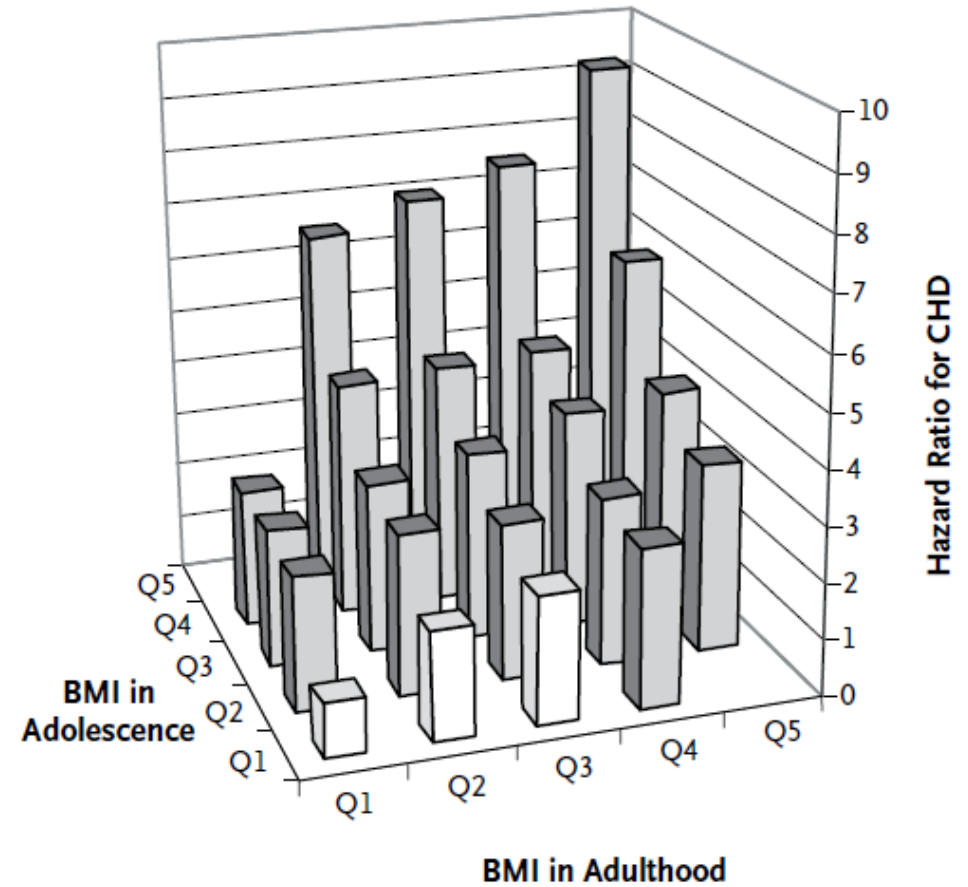
"…elevated BMI in childhood was associated with $ 2.9 in additional prescription drug, emergency room, and outpatient visit costs annually."

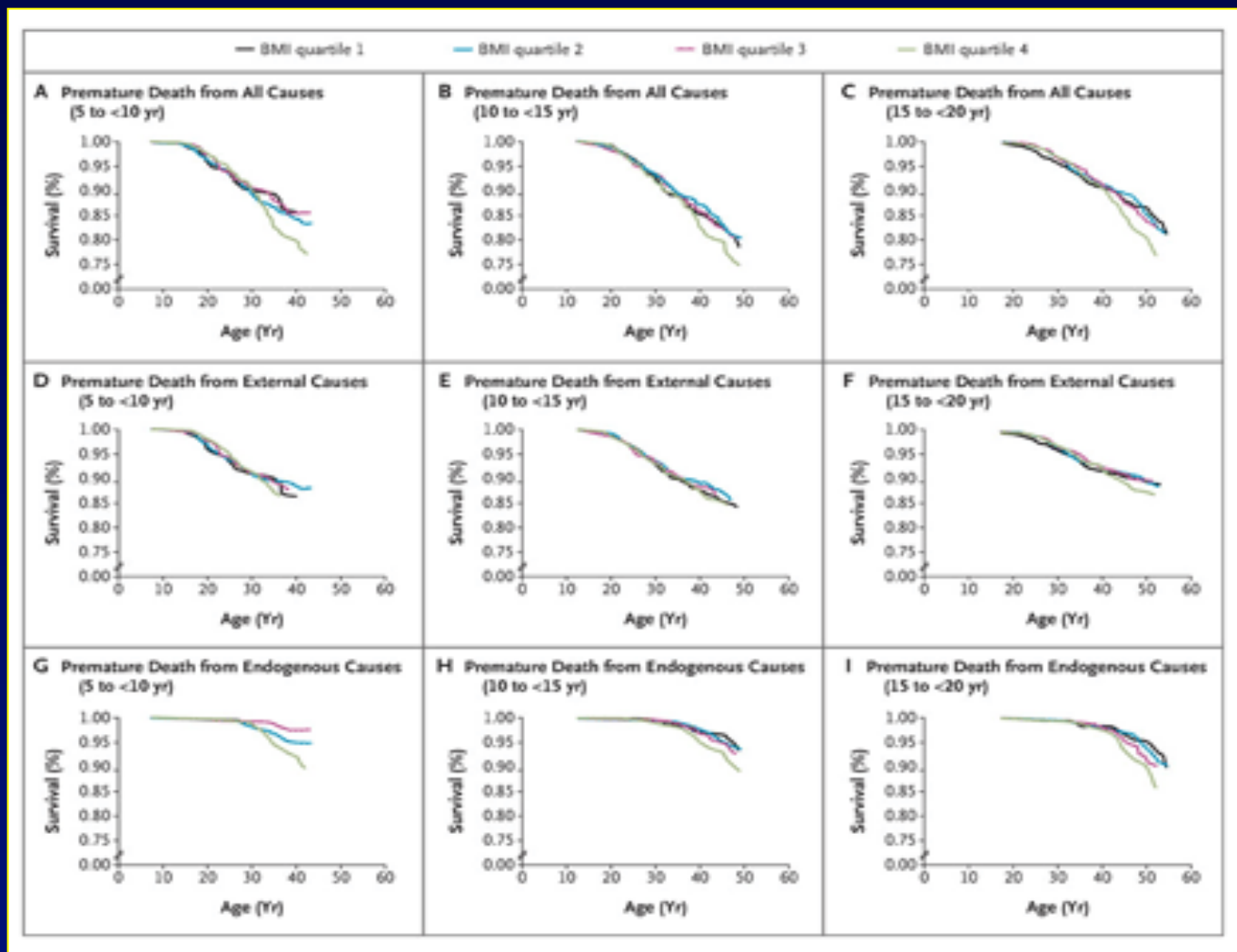
Trasande L & Chatterjee S, Obesity 2009

Establishing a standard definition for child overweight and obesity worldwide: international survey

Cole TJ *et al.*. BMJ. 2000;320(7244):1240-3

circonferenza minima della vita

Complications of Childhood Obesity
Psychosocial
Poor self esteem
Depression
Quality of life
Pulmonary
Asthma
Sleep apnea
Exercise intolerance
Renal
Glomerulosclerosis
Proteinuria
Gastrointestinal
Paniculitis
Steatohepatitis
Liver fibrosis
Gallstones
Risk for cirrhosis
Risk for colon cancer
Musculoskeletal
Forearm fracture
Blount's disease
Slipped capital femoral epiphysis
Flat feet
Risk for degenerative joint disease
Neurological
Pseudotumor cerebri
Risk for stroke
Cardiovascular
Dyslipidemia
Hypertension
Left ventricular hypertrophy
Chronic inflammation
Endothelial dysfunction
Risk of coronary disease
Endocrine
Type 2 diabetes
Precocious puberty
Polycystic ovary syndrome (girls)
Hypogonadism (boys)
Hernia
DVT/PE
Stress incontinence
Risk of GYN malignancy

Adolescent BMI Trajectory and Risk of Diabetes versus Coronary Disease

Tirosh A, *et al*. NEJM 2011;364:1315-25

Childhood Obesity, Other Cardiovascular Risk Factors, and Premature Death

Franks PW, et al NEJM 2010

Physical characteristics of children divided into normal weight, overweight, and obese

Girls

	Normal weight (n = 501)	**Overweight (n = 116)**	**Obese (n = 122)**	***P***
Age (years)	10.7 (2.1)	10.4 (2.1)	10.5 (2.2)	NS
BMI (kg/m^2)	17.2 (2.1)	21.8 (2.2)	28.7 (4.3)	<.001
BMI *z* score	–0.4 (0.8)	1.3 (0.4)	2.6 (0.5)	<.001
Waist circumf. (cm)	59.1 (6.2)	68.6 (7.1)	84.9 (10.8)	<.001
Systolic bp (mm Hg)	109.2 (12.9)	114.1 (12.1)	117.8 (13.5)	<.001
Diastolic bp (mm Hg)	65.3 (10.4)	70.2 (10.1)	70.4 (9.8)	<.001
Triacylglycerol (mg/dL)	66.3 (26.1)	78.4 (41.1)	100.3 (59.8)	<.001
HDL cholesterol (mg/dL)	59.1 (13.8)	53.5 (13.4)	46 (11.8)	<.001
Glucose (mg/dL)	88.3 (8.3)	87.9 (8.4)	87.8 (8.3)	NS

Maffeis C, *et al.* J Pediatr 2008

Metabolic Syndrome Factor Structure Analysis

obesity

waist

BMI

IGT

insulin

glucose

dyslipidemia

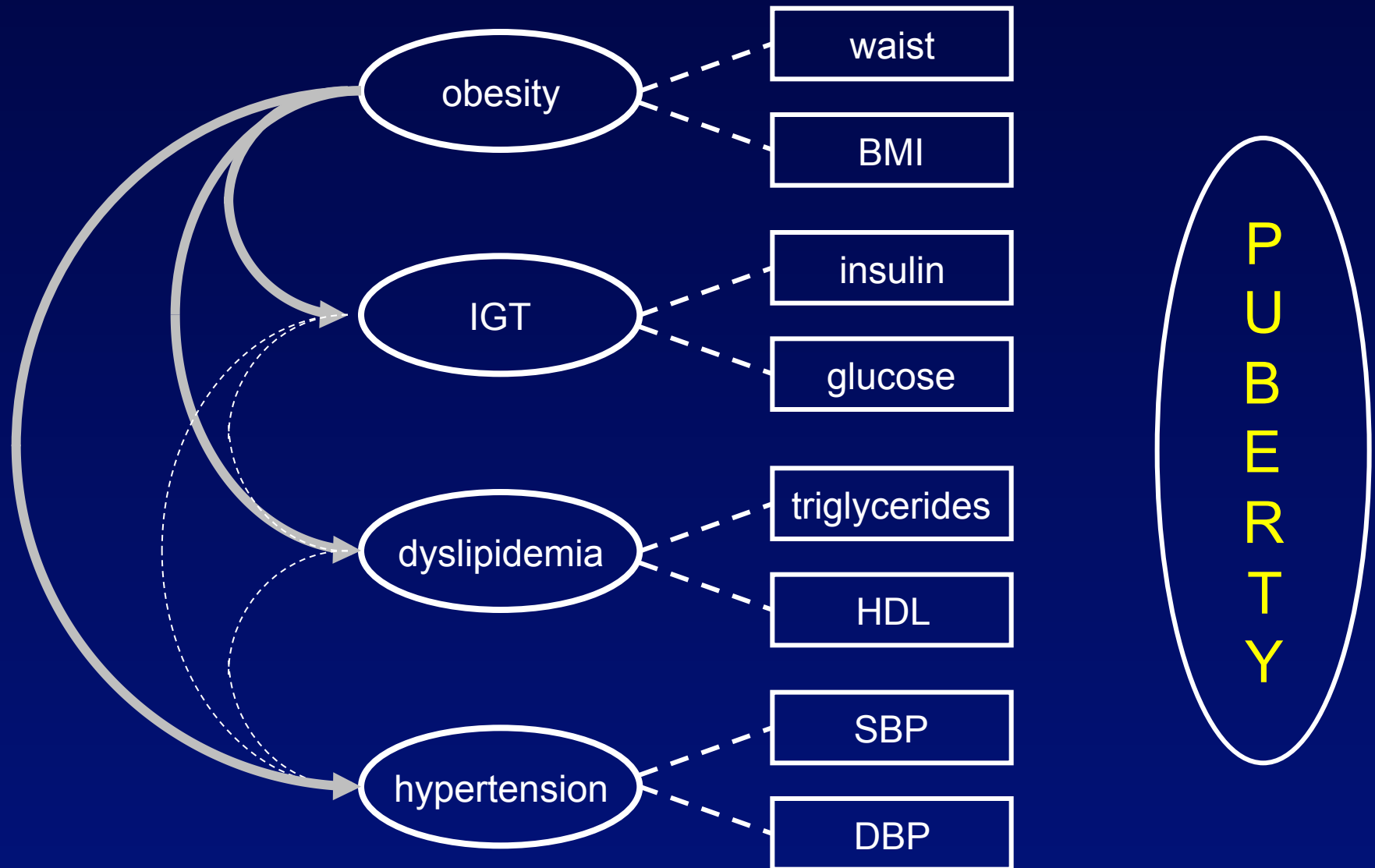
triglycerides

HDL

hypertension

SBP

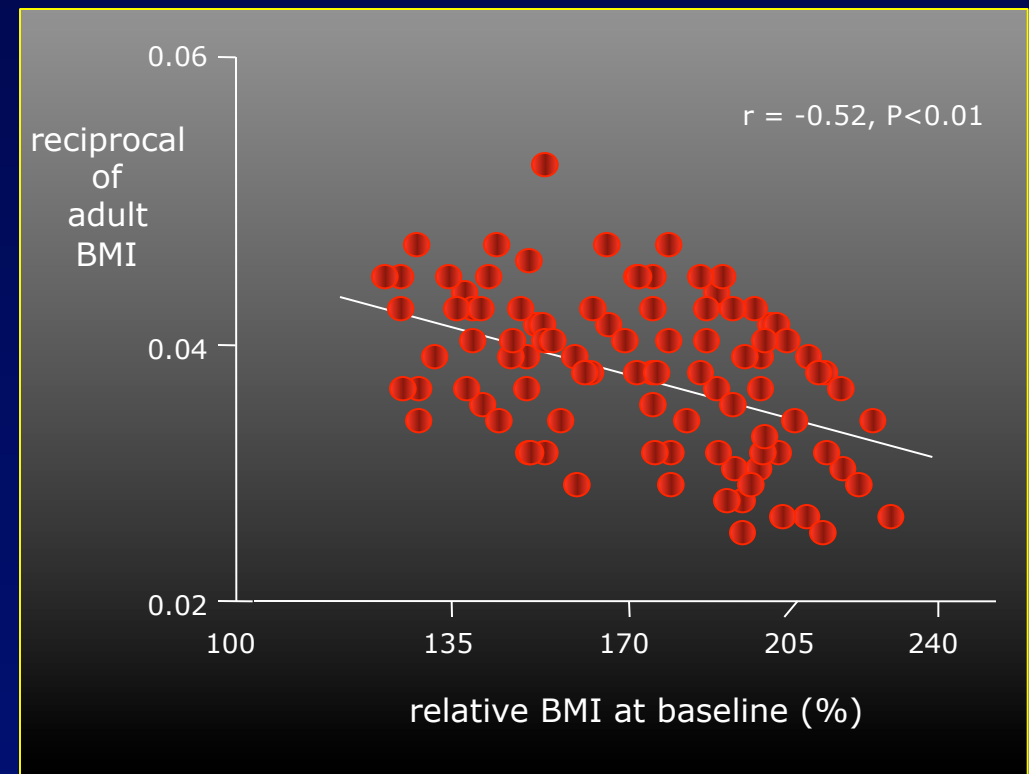
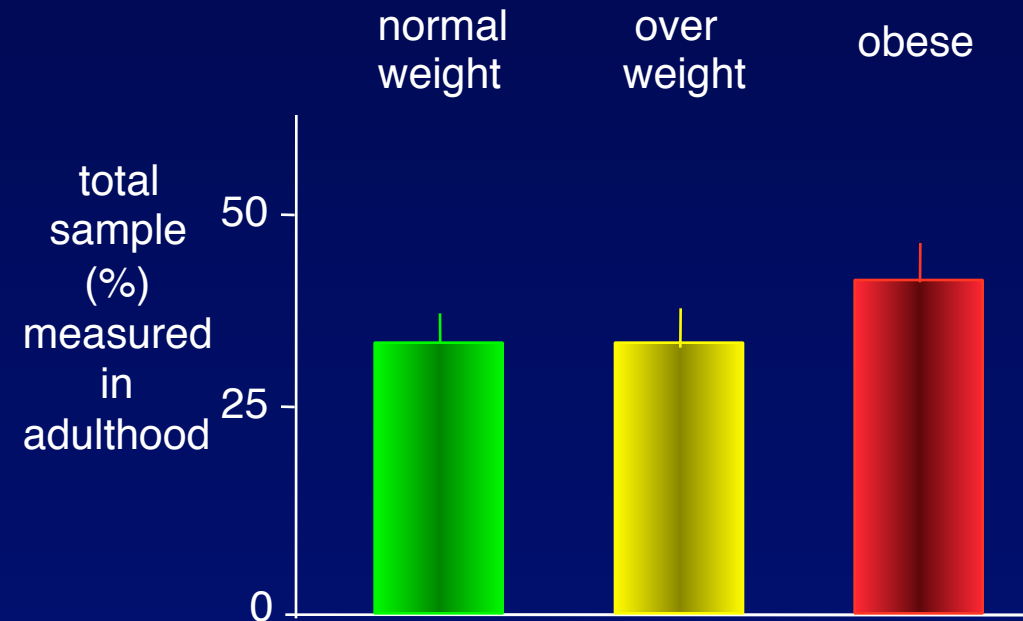
DBP

Goodman E, *et al* J Pediatr 2009

Prevalence of the Metabolic Syndrome in US Adolescents

	Cook/Ford % (SE)	Cruz % (SE)	Caprio % (SE)	Adult % (SE)
Overall	9.4 (1.2)	2.0 (0.4)	2.4 (0.4)	5.8 (0.9)
Gender				
Male	13.2 (2.0)	3.0 (0.8)	3.8 (0.8)	7.0 (1.4)
Female	5.3 (1.2)	1.0 (0.4)	0.6 (0.3)	4.5 (1.2)
Race/Ethnicity				
White	10.7 (1.9)	2.2 (0.5)	2.5 (0.6)	6.0 (1.4)
Black	5.2 (1.1)	1.6 (0.5)	1.9 (0.7)	4.7 (1.1)
Mex.-Am-Hisp.	11.1 (1.2)	2.6 (0.6)	3.1 (0.7)	6.0 (0.9)
BMI status				
Normal	1.6 (0.7)	0 (0)	0 (0)	1.1 (0.5)
At risk	7.8 (3.6)	0 (0)	0 (0)	5.8 (2.8)
Overweight	44.2 (2.9)	12.4 (2.5)	14.1 (2.6)	26.2 (3.6)

Cook S, *et al* J Pediatr 2008

persistence of obesity from childhood into adulthood

Maffeis C *et al*. J Clin Endocrinol Metab 2002;87:71-76

predicted risk of having a CHD event between 25 and 60 yrs in 276,835 children of average or higher than average BMI

		weight equivalent to a BMI z score of 0 (kg)	RR of an event with 1-Unit increase in BMI z score (95% CI)	event by 60 yr of age (estimated percentage)	
				BMI z score:	
				0	2
BOYS	7 yr	23.7	1.06 (1.04-1.08)	11.7	12.9
	13 yr	43.8	1.17 (1.15-1.20)	11.7	15.5
GIRLS	7 yr	23.3	1.02 (0.99-1.06)	4.6	4.8
	13 yr	45.7	1.12 (1.09-1.16)	4.6	5.7

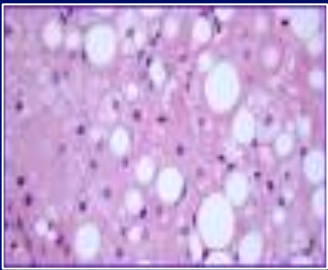
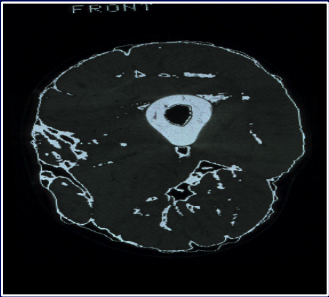
Baker et al. NEJM 2007;357:2329-37.

Type 2 Diabetes & Impaired Glucose Tolerance in European children and adolescents with obesity

	ADA criteria (# of subjects)	WHO criteria (# of subjects)
Impaired fasting glucose	12	12
Impaired glucose tolerance		37
Type 2 Diabetes Mellitus	2	6
Normal glucose regulation	88	56
Total	102	102

Wiegand S *et al.* EJE 2004

OBESITY

ECTOPIC FAT ACCUMULATION

Franzese A, Vajro P, et al.

Dig Dis Sci 1997

INFLAMMATION

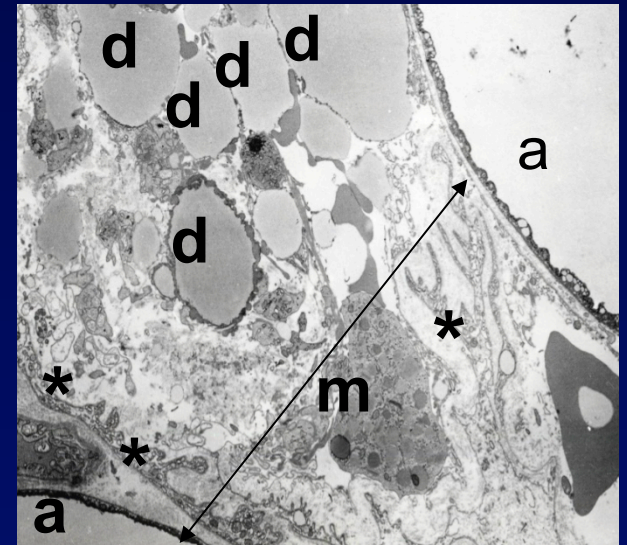
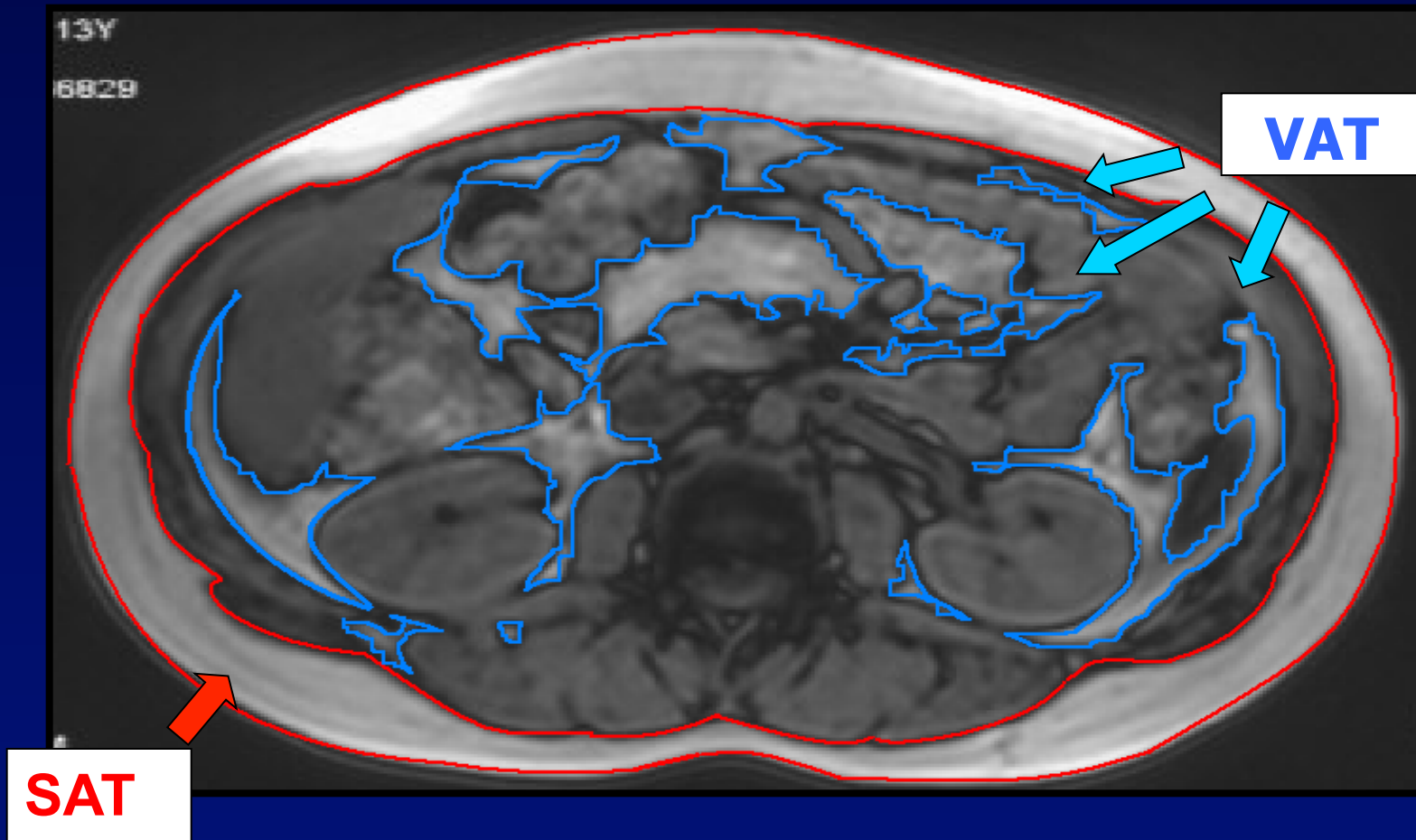
Sbarbati M, Maffeis C, et al.
Pediatrics 2006

INSULIN RESISTANCE

Hypertension

dislipidemia

IGT – T2D

METABOLIC SYNDROME

10-year-old obese boy: MRI L4
VAT: visceral adipose tissue
SAT: subcutaneous adipose tissue

Odds ratio to have the metabolic syndrome in subjects with a W/Hr >0.5 within normal-weight, overweight, and obese BMI categories

Childhood Obesity Group of the Italian Society of Pediatric Endocrinology & Diabetology

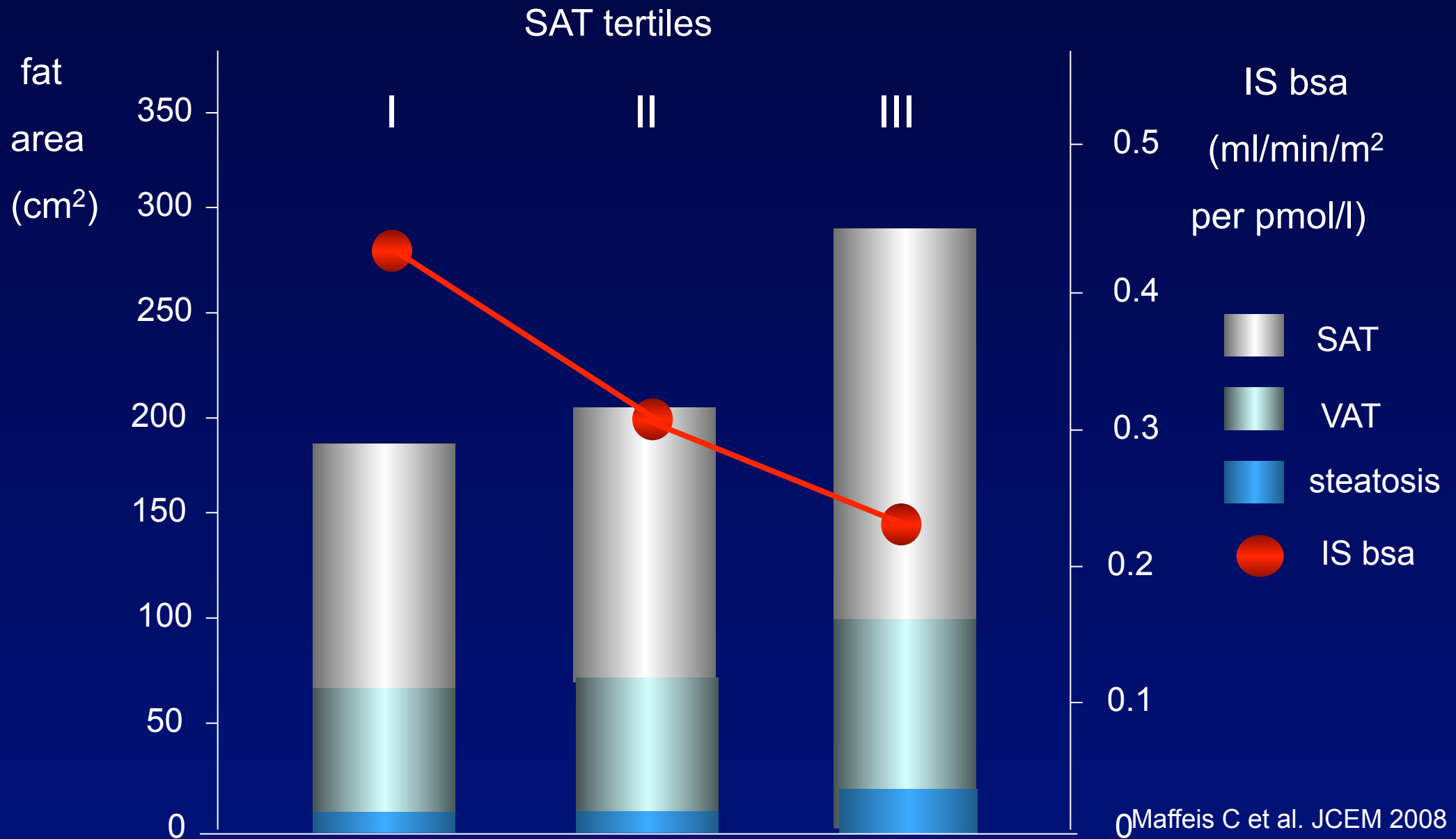
W

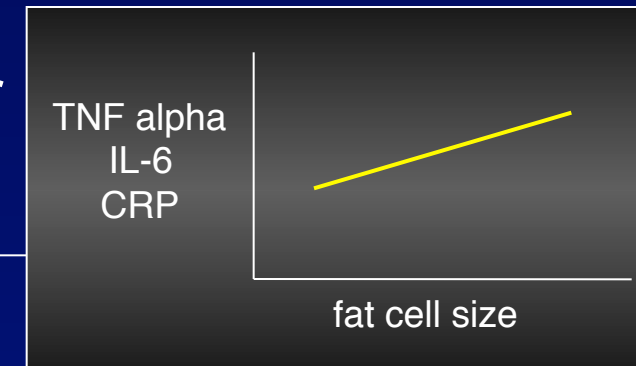
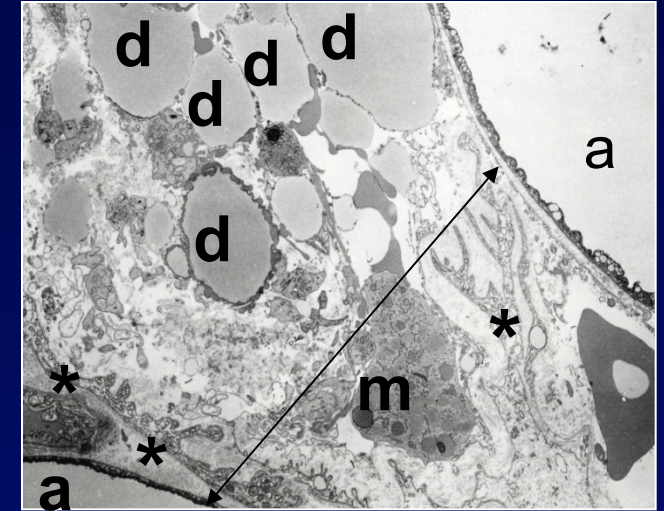
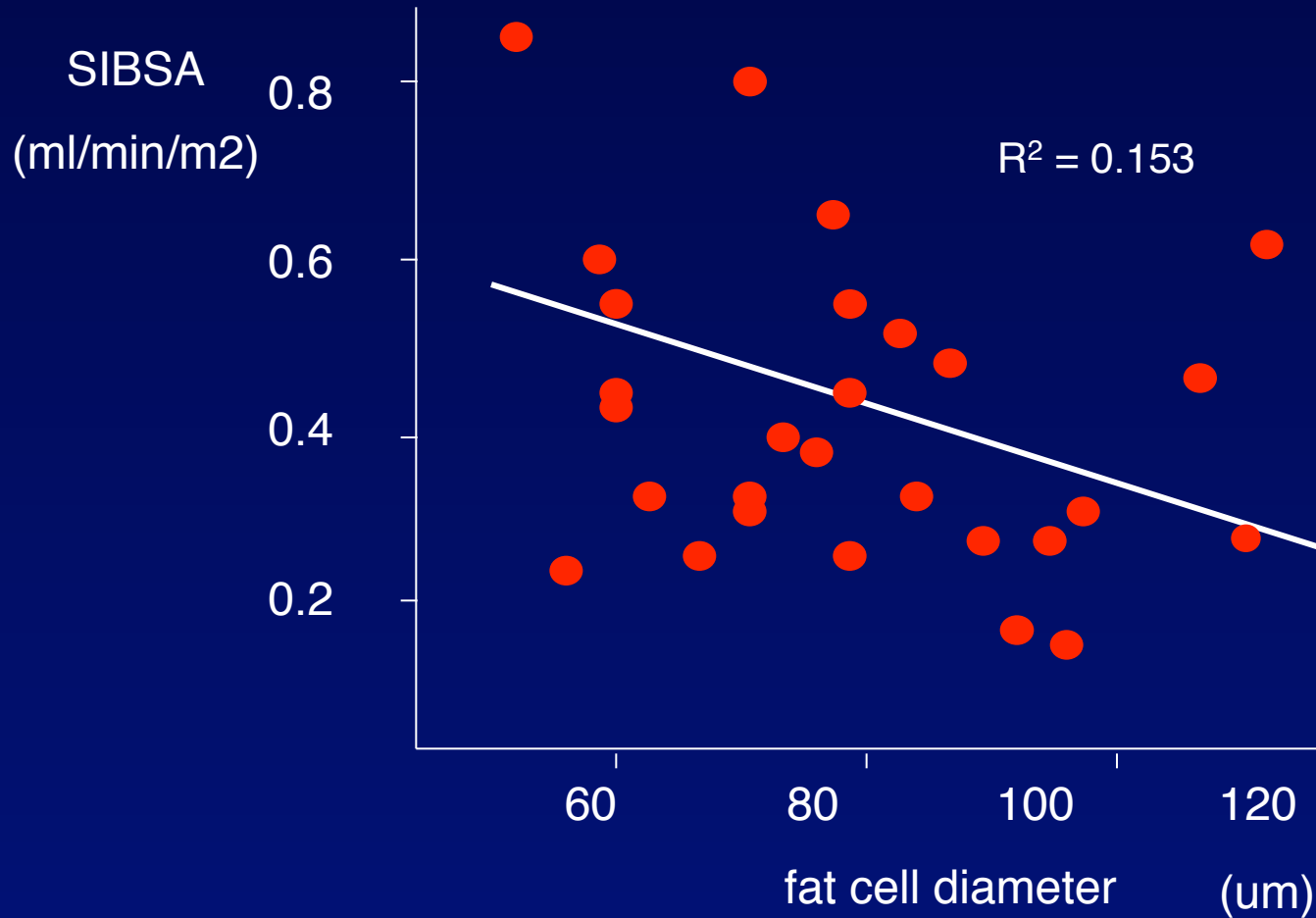
H

	Metabolic syndrome		Risk to develop metabolic syndrome
Independent variables	**No**	**Yes**	**OR (95% CI)**
Normal weight with W/Hr <0.5	938	22	1
Normal weight with W/Hr >0.5	13	1	4.01 (0.49-32.97)
Over weight with W/Hr <0.5	132	10	3.34 (1.52-7.37) *
Over weight with W/Hr >0.5	72	16	8.16 (3.87-17.23) **
Obese with W/Hr >0.5	208	67	12.11 (7.08-20.71) **

*W/Hr = waist/height ratio * $P < .05$. ** $P < .001$.*

Maffeis C, *et al.* J Pediatr 2008

insulin sensitivity, abdominal fat distribution and liver steatosis in prepubertal children

adipocyte size, insulin sensitivity and inflammation in overweight and obese pre-pubertal children

Maffeis C, *et al.* J Pediatr 2007 and Pediatrics 2006

presence of increased stiffness of the common carotid artery and endothelial dysfunction in severely obese children: a prospective study

Severe obesity in children is associated with arterial wall stiffness and endothelial dysfunction.

obese vs nonobese children:

lower arterial compliance
lower distensibility
higher values for wall stress and incremental elastic modulus
lower endothelium-dependent & independent function

Tounian P, *et al.* Lancet 2001

obesity:

congenital leptin deficency

Montague CT, *et al.* Nature. 1997;387:903-8

heritability of BMI is about 25-50%

430 genes, markers and chromosomal regions potentially involved

parental and perinatal factors associated with childhood obesity in north-east Italy

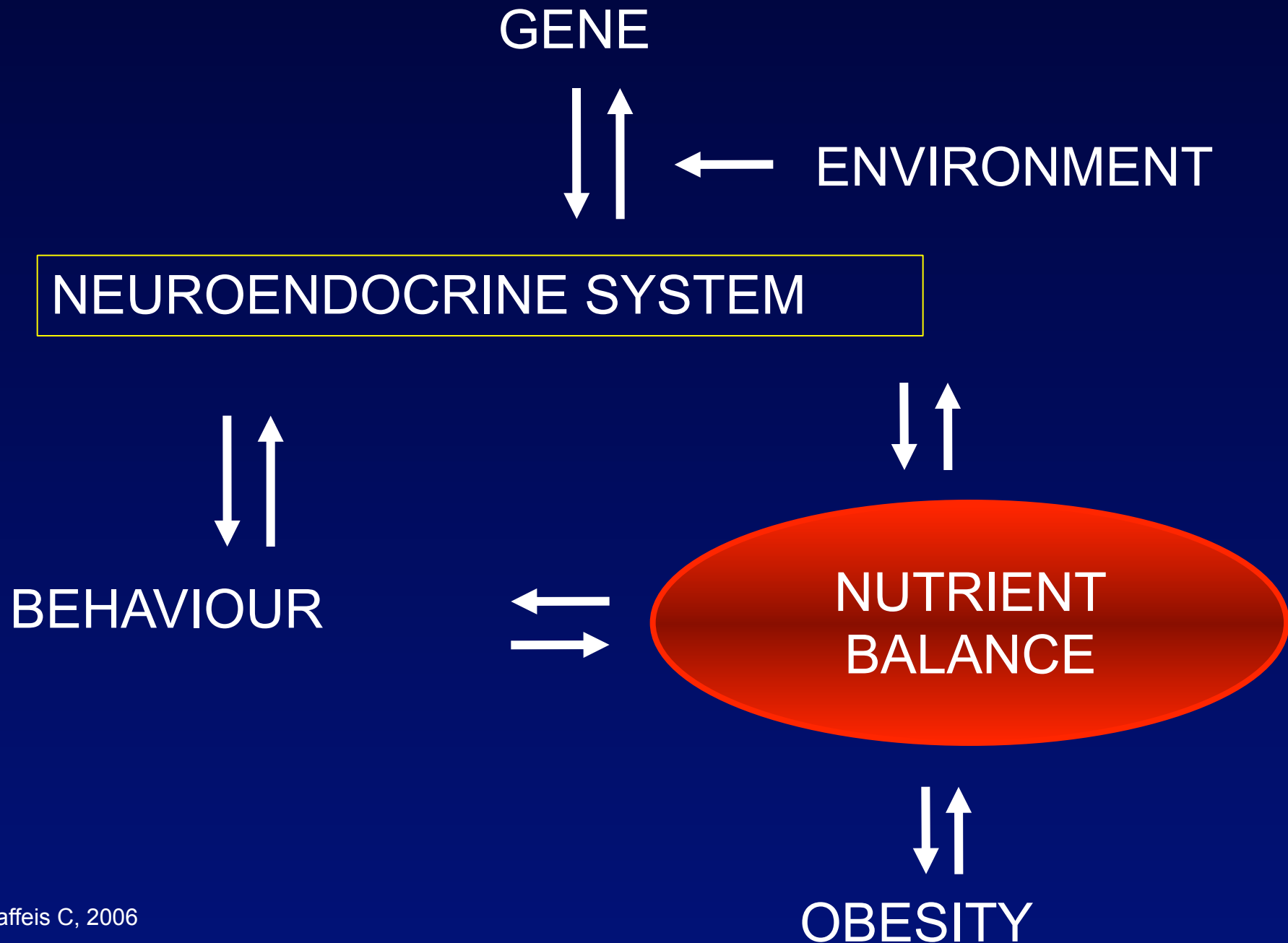
"… When parental and perinatal variables were included as independent variables in a multiple logistic regression model controlling for the effect of age, *parental body mass index* and *children's birth-weight* remained independently associated with childhood obesity. "

Maffeis C, *et al.* Int J Obes 1994;18:301-5.

GENE

ENVIRONMENT

OBESITY

Maffeis C, 2006

Stressing the Brain, Fattening the Body

Hypothalamic IKKb/NF-kB and ER
Stress Link Overnutrition to Energy Imbalance and Obesity

Zhang X, et al. Cell 2008

skeletal muscle

↑ VAT

① insulin resistance

liver

③ insulin resistance

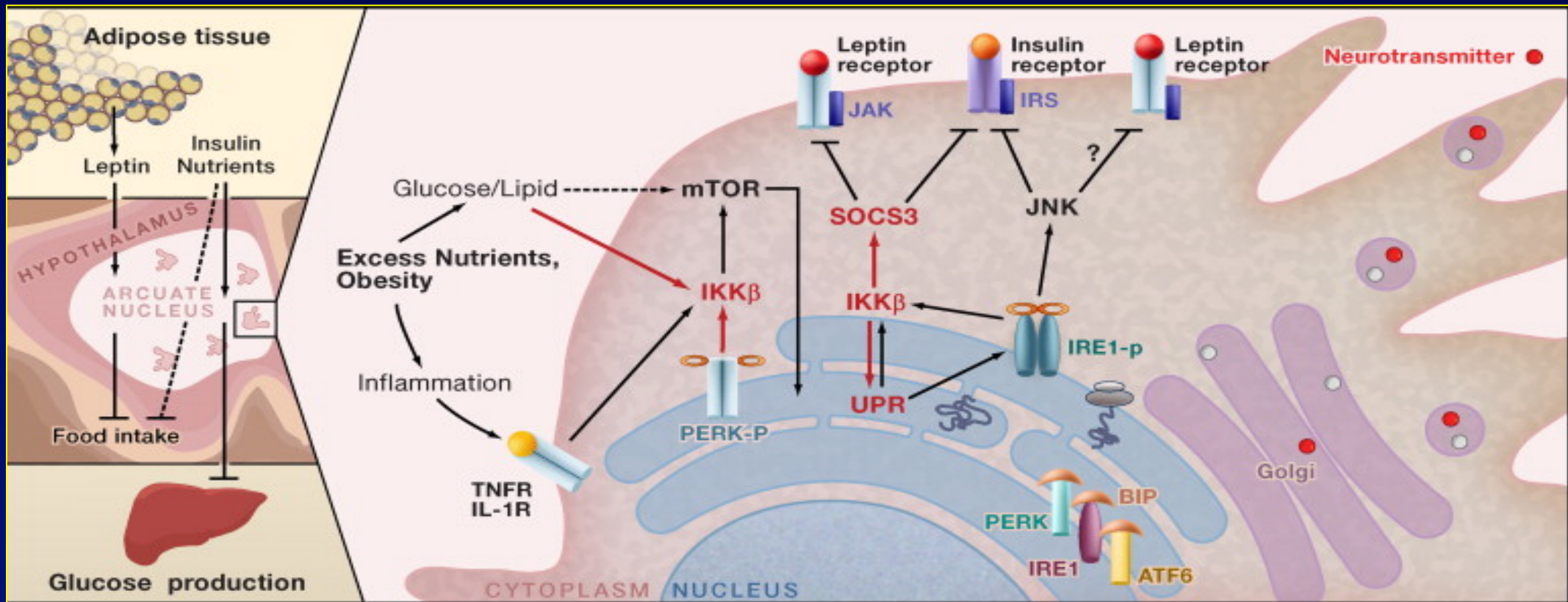
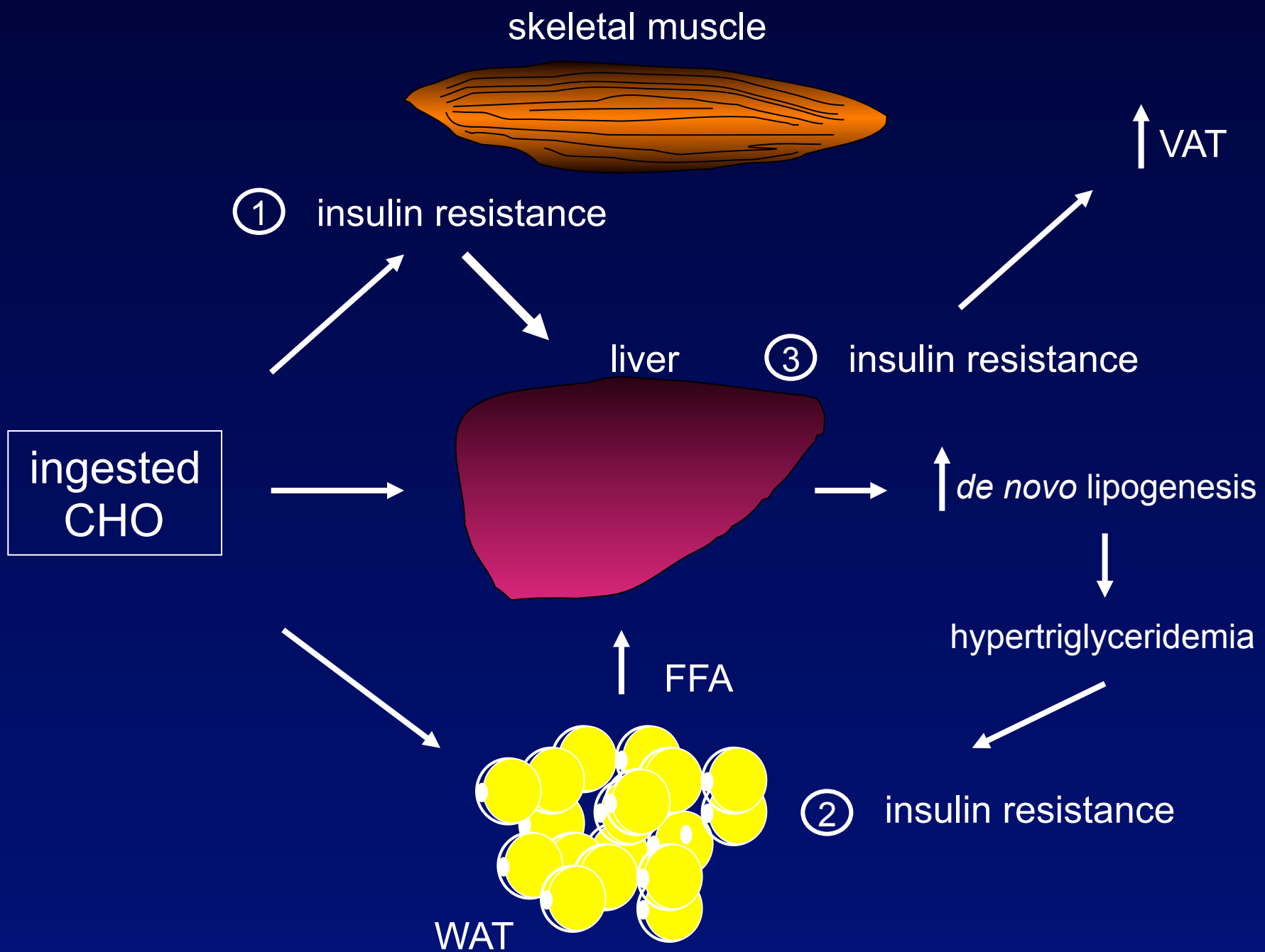
ingested CHO

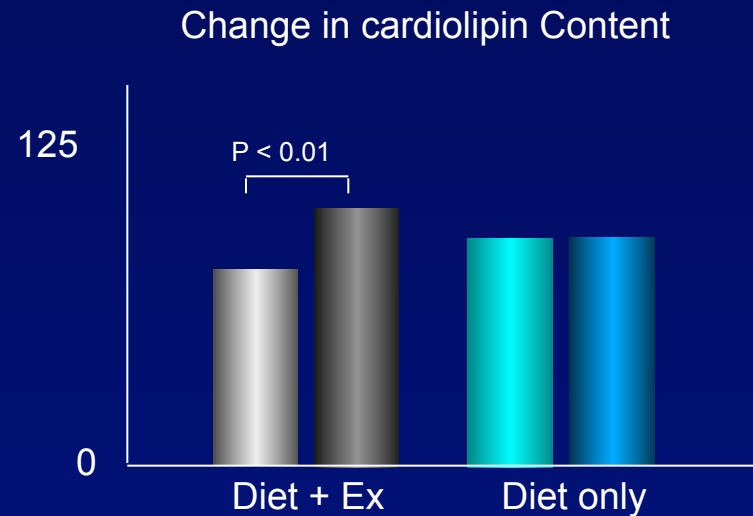
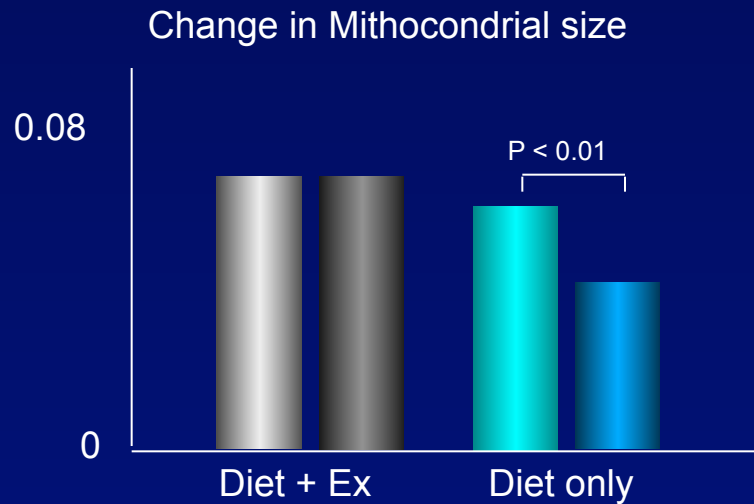
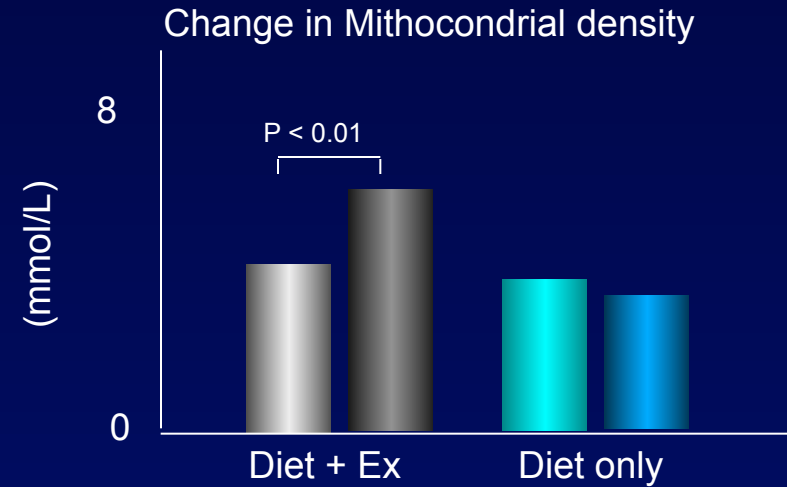
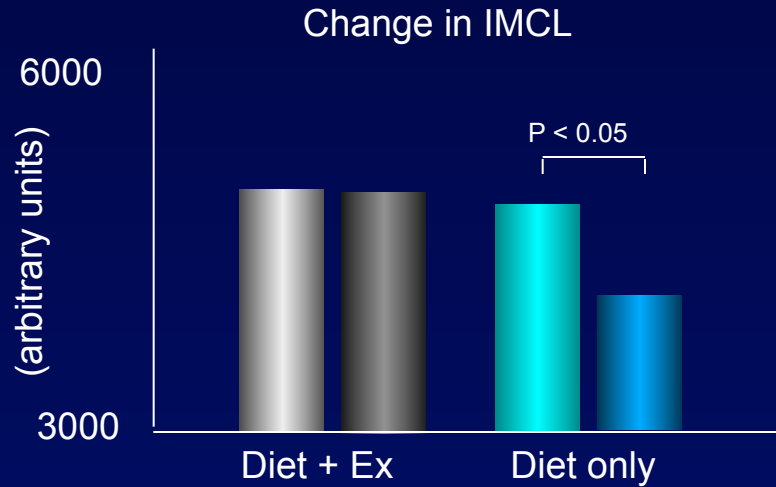
↑ *de novo* lipogenesis

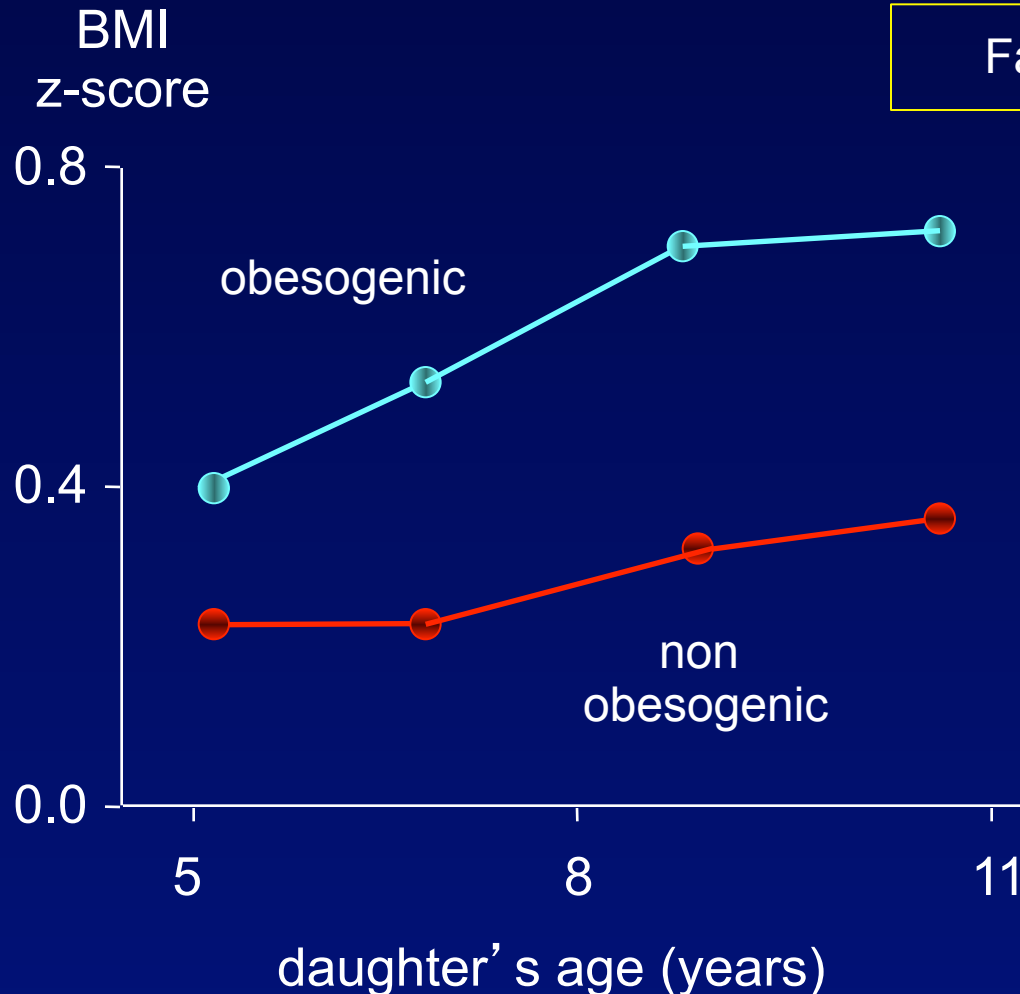
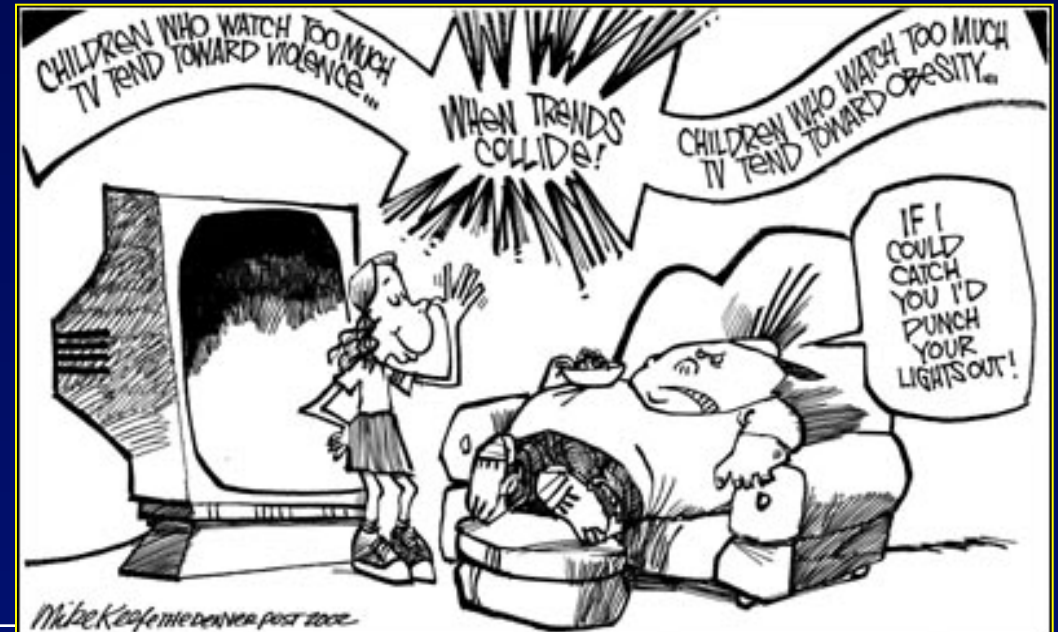
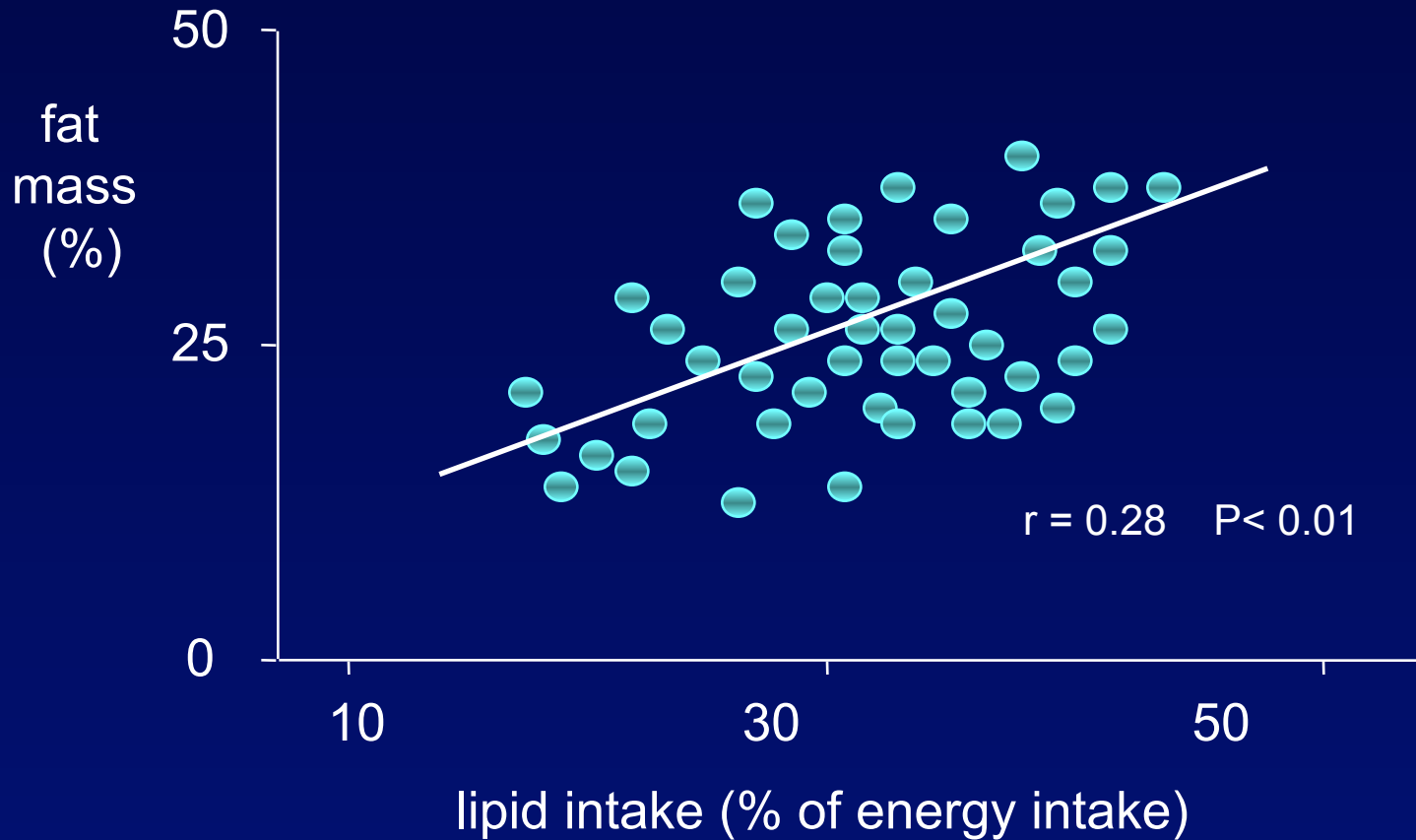
hypertriglyceridemia

↑ FFA

② insulin resistance

WAT

mitochondrial capacity in skeletal muscle is not stimulated by weight loss despite increases in insulin action and decreases in intramyocellular lipid content

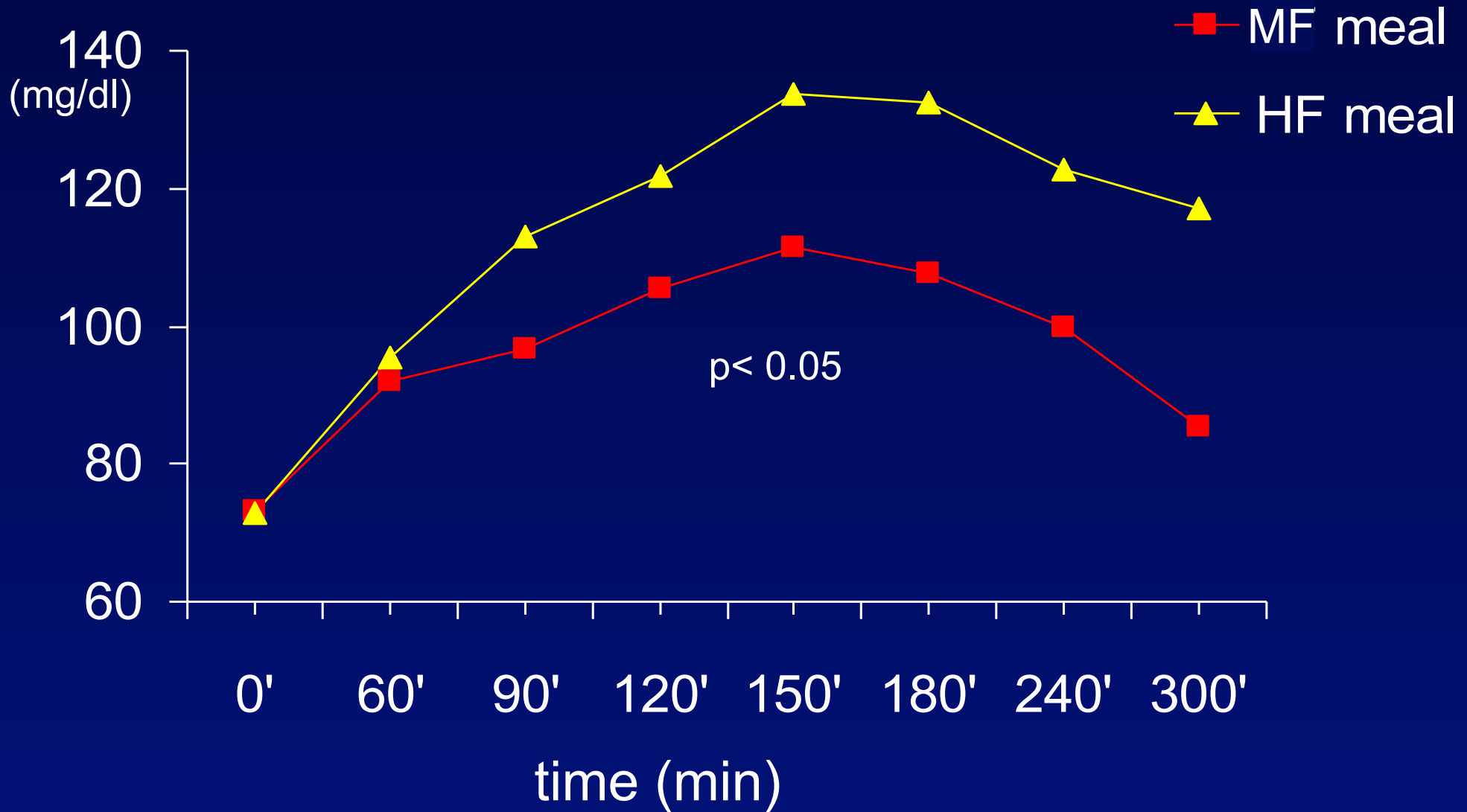
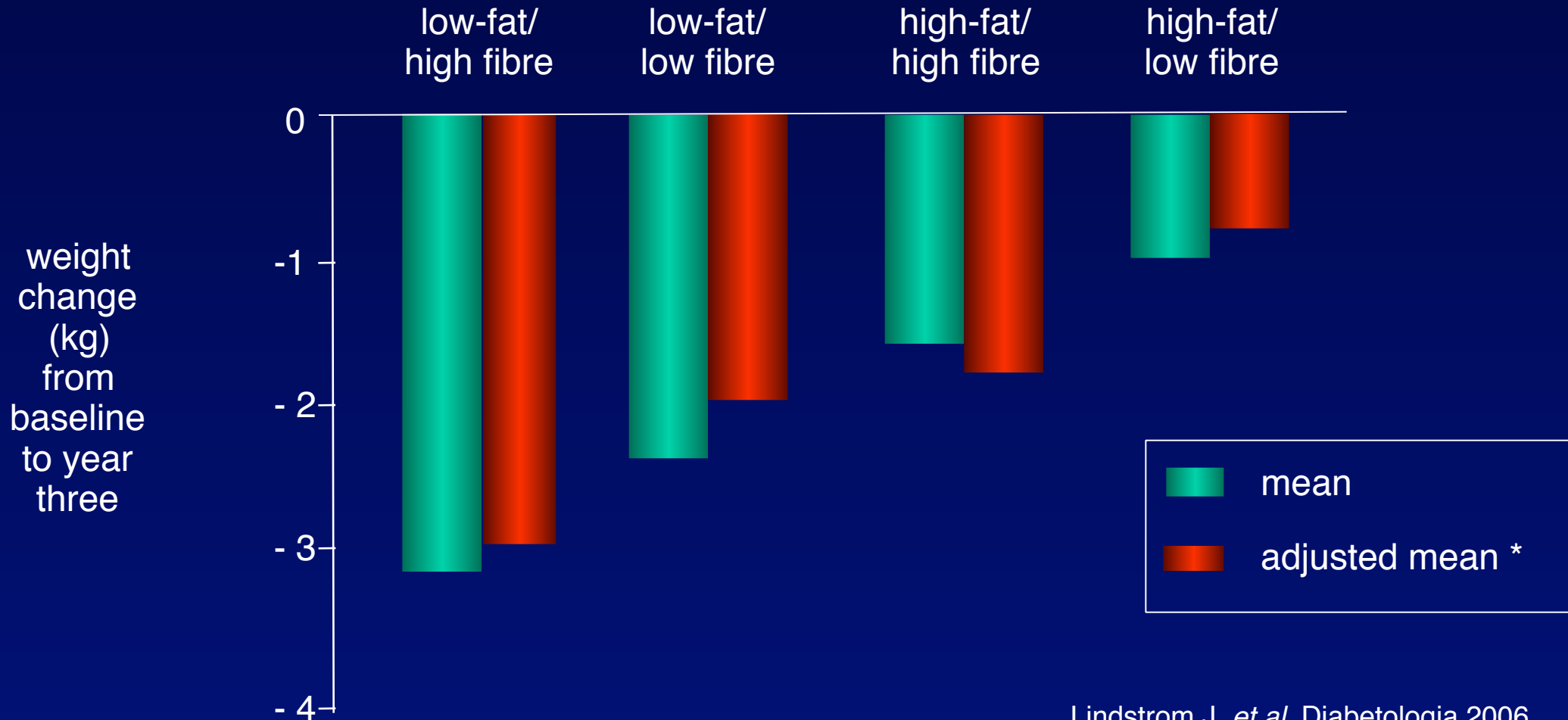
Toledo FGS, et al. Diabetes 2008

association of family environment with children's TV viewing and with low levels of physical activity

Davidson KK, *et al*. Obes Res 2005

relationship between fat in the diet and fat mass

Klesges RC *et al.* AJCN ‘94

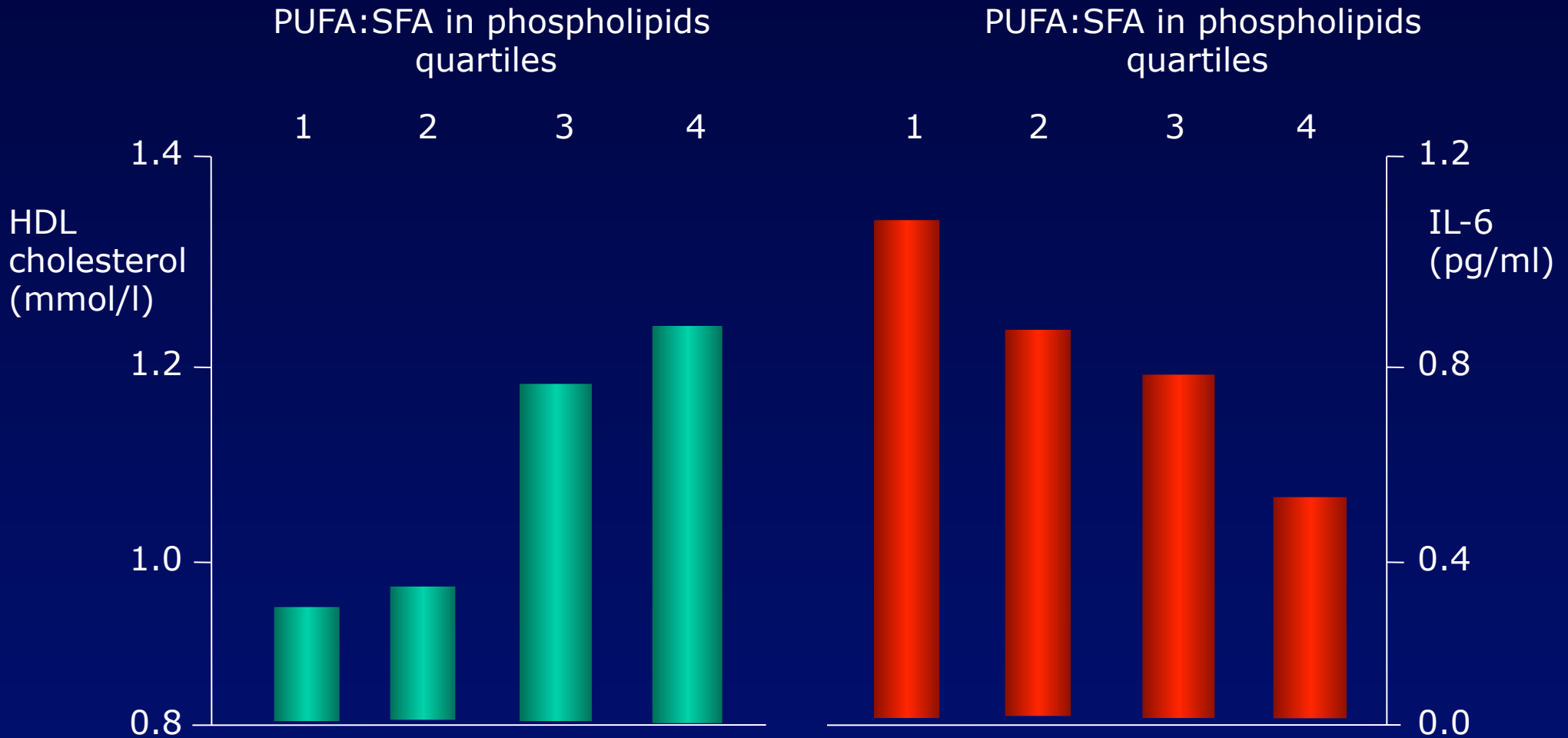
Gazzaniga JM, *et al.*AJCN ‘93

Maffeis C *et al.* Int J Obes ‘96

postprandial triglycerides changes after a moderate fat and a high fat meal

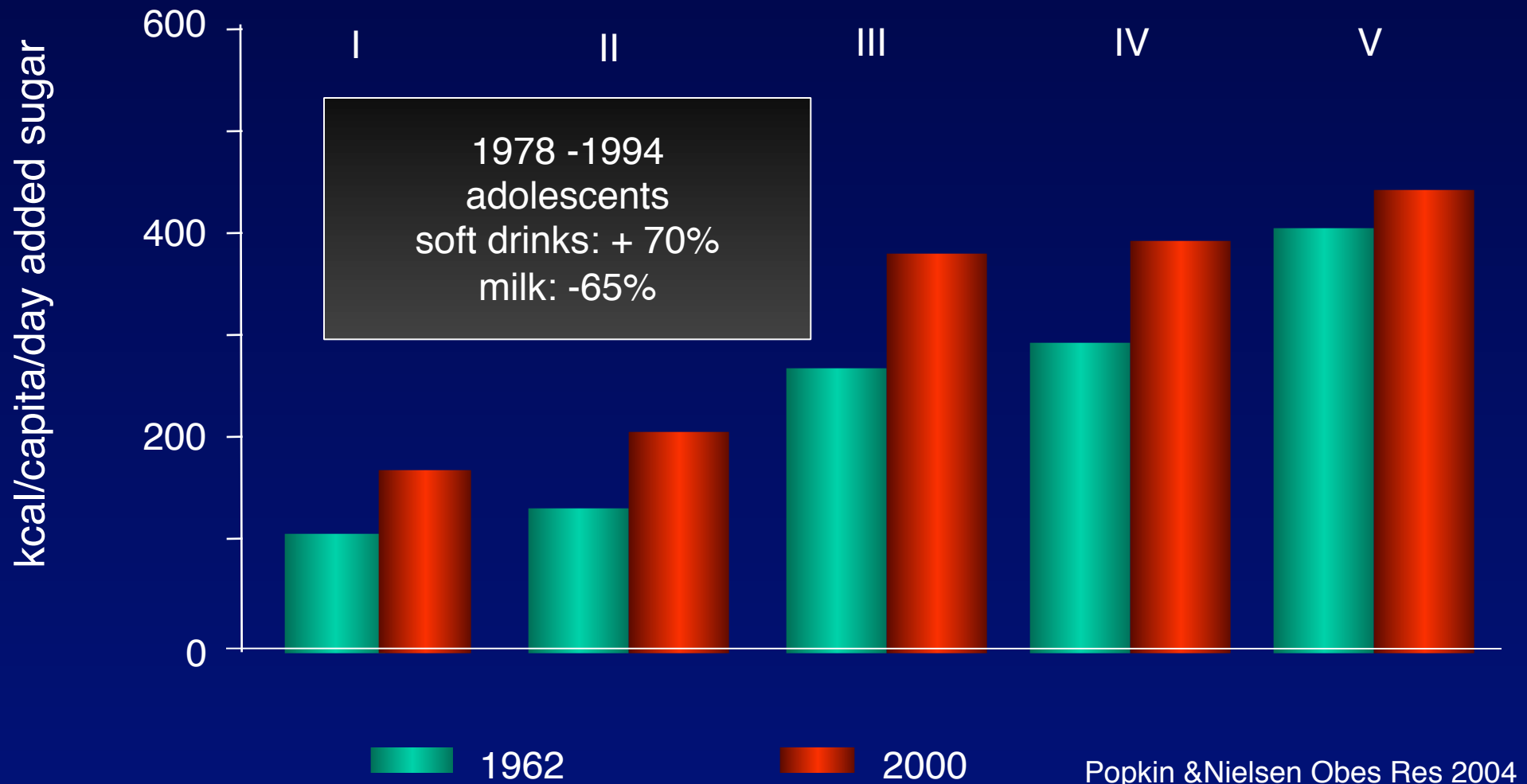
Maffeis C, *et al*. Obesity 2009

high-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study

Lindstrom J, *et al*. Diabetologia 2006

* group assignment, age, sex, baseline BW, fat, fibre, VLDL-use, & baseline and follow-up period physical activity

fatty acids, inflammation, and the metabolic syndrome

Dietary intakes of fat and antioxidant vitamins are predictors of subclinical inflammation in overweight Swiss children

Aeberli I, et al AJCN 2006

THE SWEETING OF THE WORLD' S DIET

Popkin &Nielsen Obes Res 2004

DECLINE IN PHYSICAL ACTIVITY DURING ADOLESCENCE

Kimm SYS, et al. N Engl J Med 2002

fat mass (%)

50

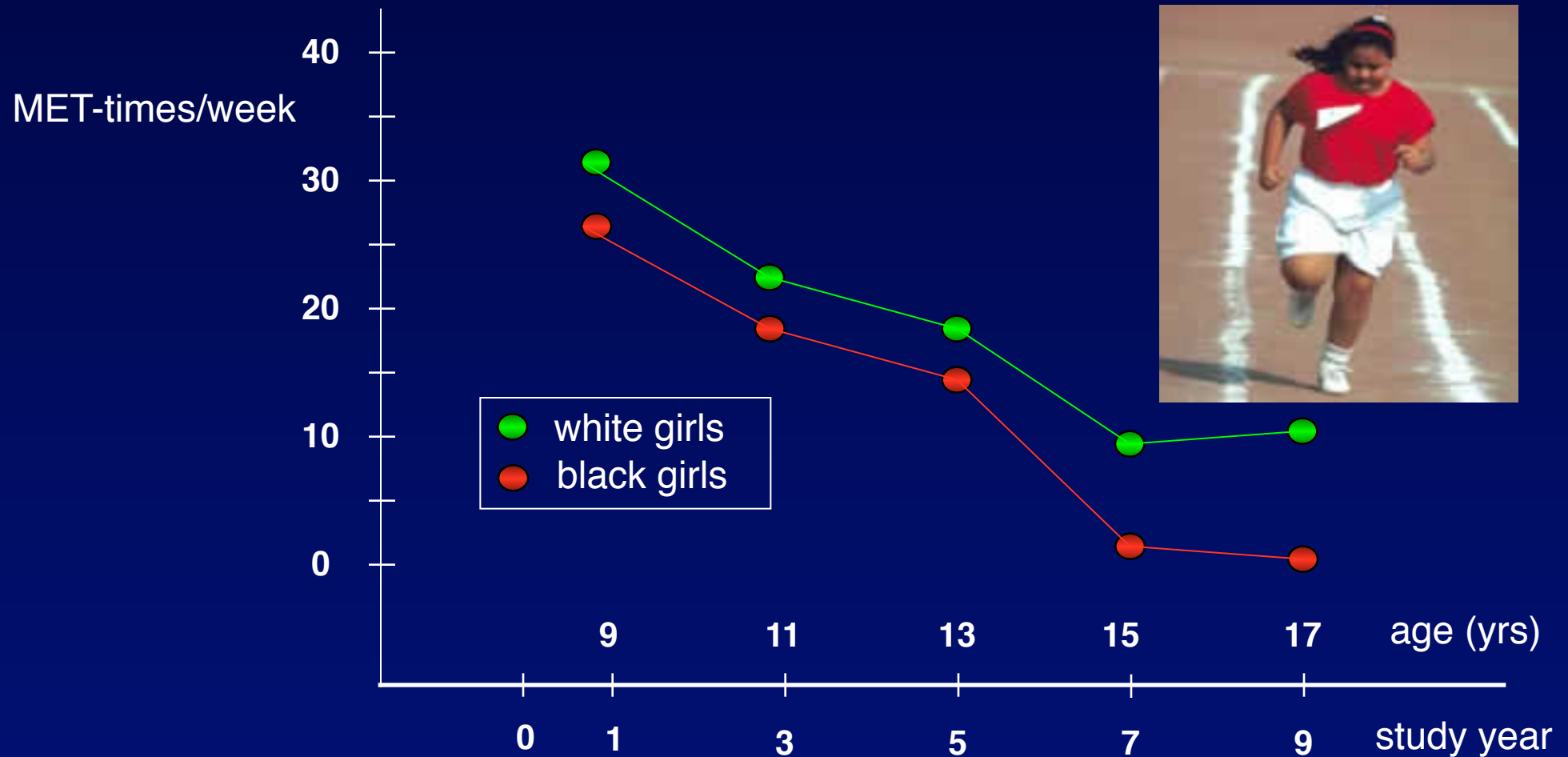
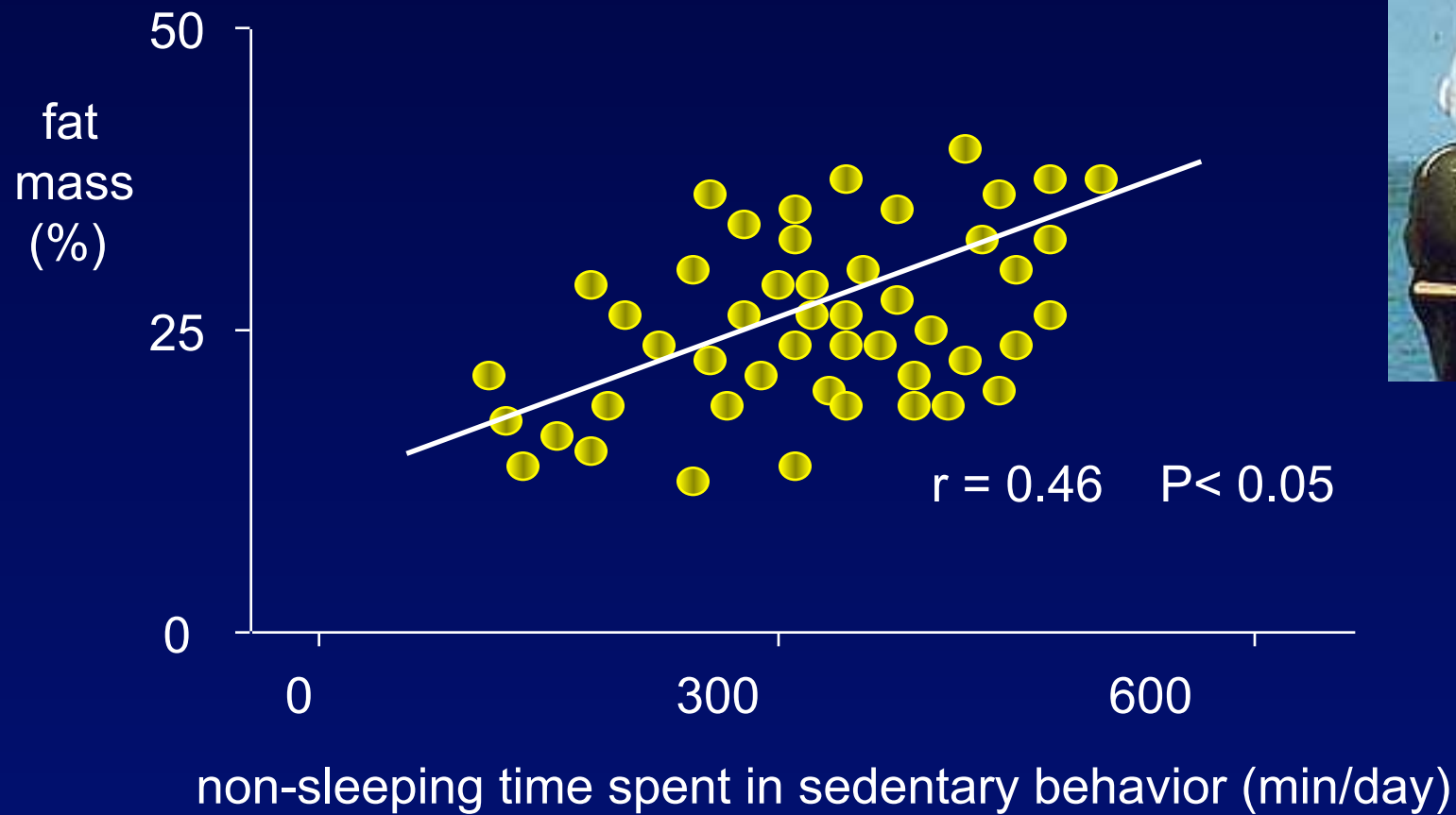
25

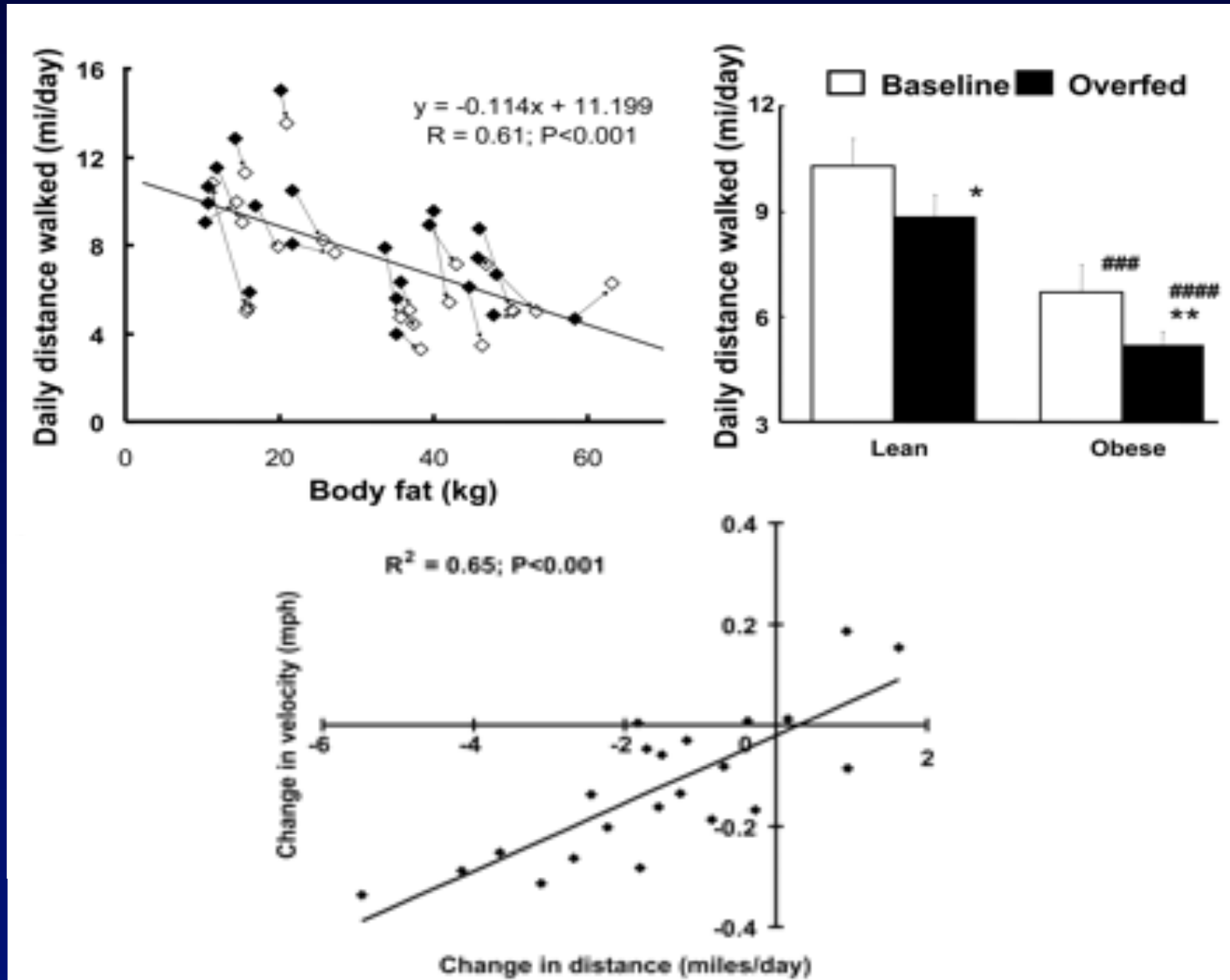
0

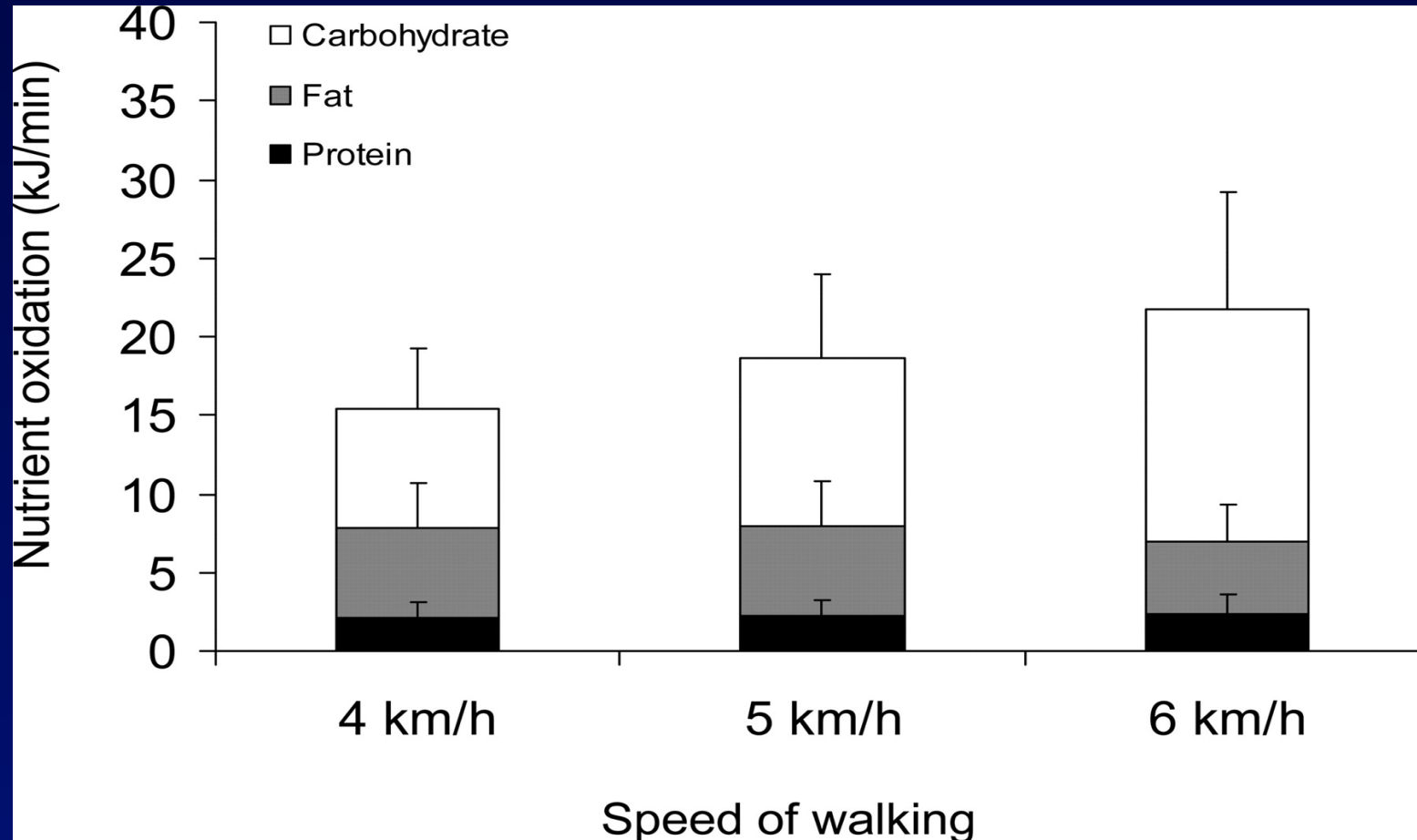
0 300 600

non-sleeping time spent in sedentary behavior (min/day)

r = 0.46 P< 0.05

Maffeis C *et al.* J Pediatr ‘97

the role of free-living daily walking in human weight gain and obesity

Levine JA *et al*. Diabetes 2008

Nutrient oxidation measured during walking at speeds of 4, 5, and 6 km/h, respectively, in a group of obese prepubertal children

Maffeis, C. *et al.* JCEM 2005;90:231-236

adipocyte differentiation

multipotent mesenchymal stem cell

determined unipotential preadipocyte

immature multilocular adipocyte

mature adipocyte

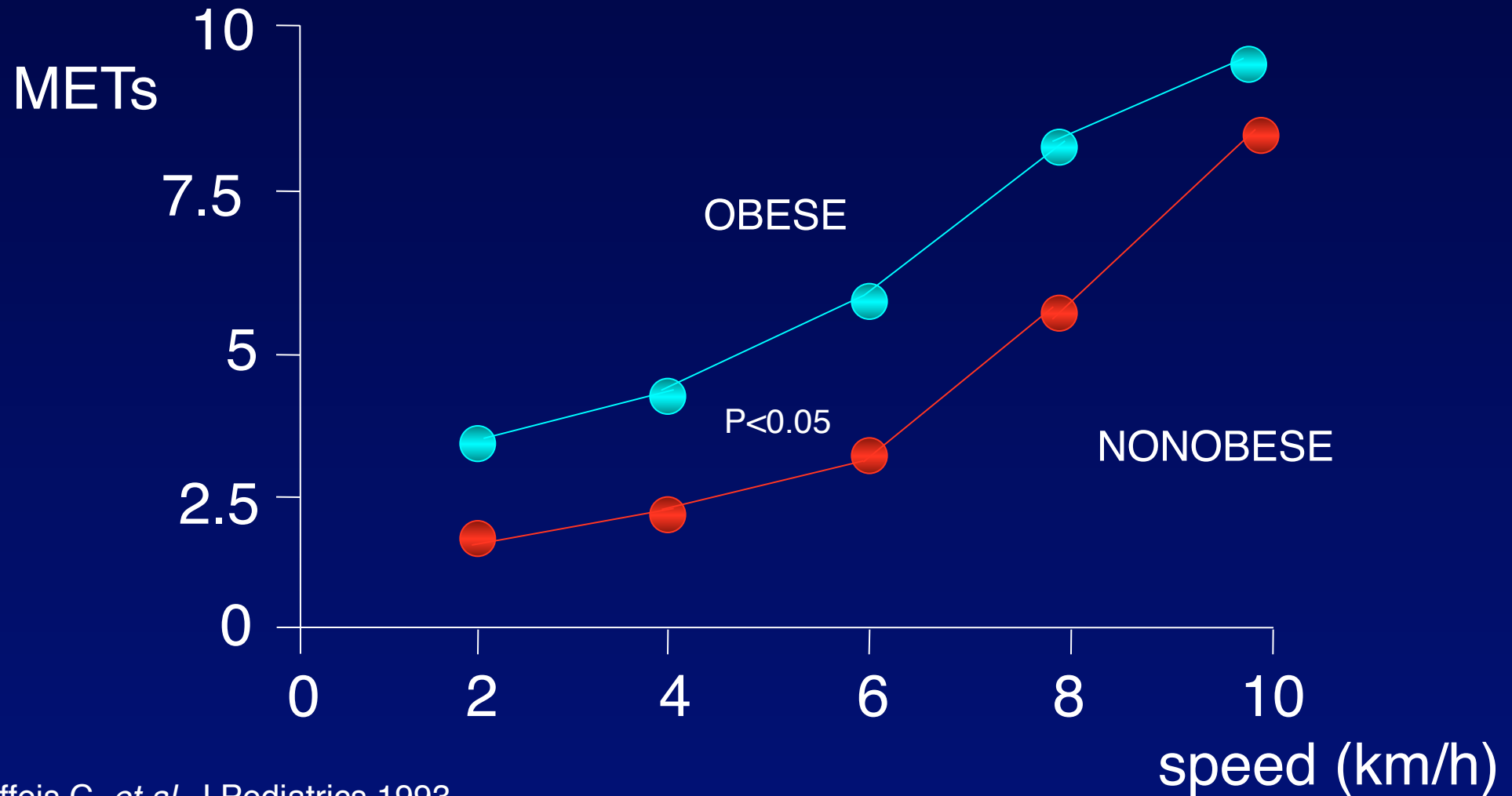
Healthy Eating Pyramid
Use Sparingly
Red Meat; Butter
White Rice, White Bread, Potatoes and Pasta; Sweets
Multiple Vitamins for Most
Dairy or Calcium Supplement, 1-2 times/day
Fish, Poultry, Eggs. 0-2 times/day
Alcohol in Moderation (unless contraindicated)
Nuts, Legumes, 1-3 times/day
Vegetables (in abundance)
Fruits, 2-3 times/day
Whole Grain Foods (at most meals)
Plant oils, including olive, canola, soy, corn, sunflower, peanut and other vegetable oils
Daily Exercise and Weight Control

bambino di 10 anni, peso 40 kg

	sedentario	non sedentario
scuola (h/die)	5	5
spostamenti (h/die)	2	2
igiene e pasti (h/die)	2	2
doposcuola o compiti (h/die)	3	3
TV videogiochi (h/die)	2.5	1
sonno (h/die)	9	9
sport (h/die)	0.5	2
spesa energetica (kcal/die)	1.700	2.100

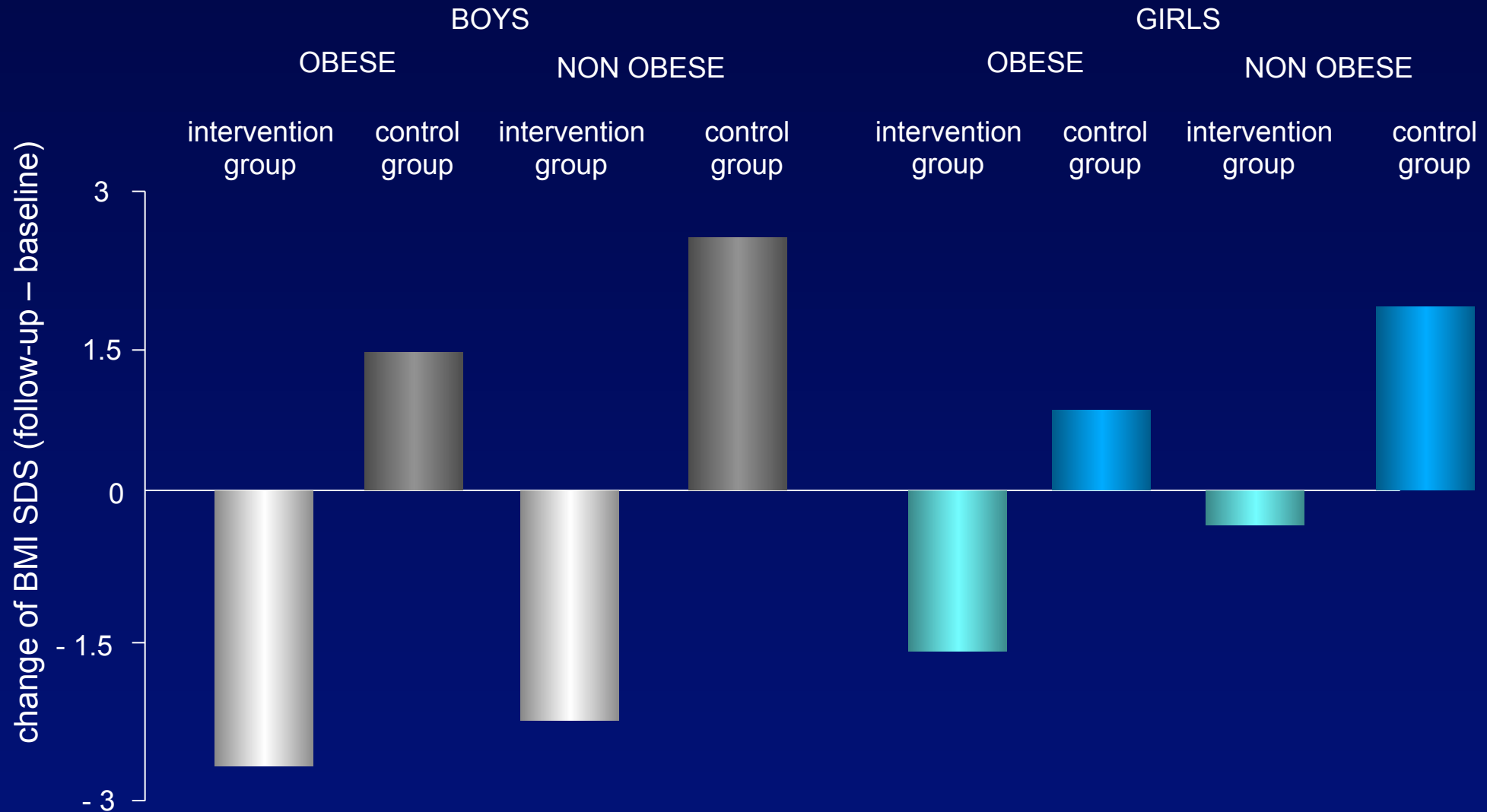
COSTO ENERGETICO DI VARIE ATTIVITA' QUOTIDIANE
bambino di 8 aa, 140 cm, 35 cm, BMI 18.

Attività	Spesa energetica (kcal/min)
Seduto a riposo (disegna, scrive)	1
Videogioco, TV	0.9
Cammina (3 km/h)	2
Cammina (3km/h + zaino)	3
Cammina (5 km/h)	4
Corre (8 km/h)	6
Sport moderata intensità (nuoto, sport di squadra)	4-5

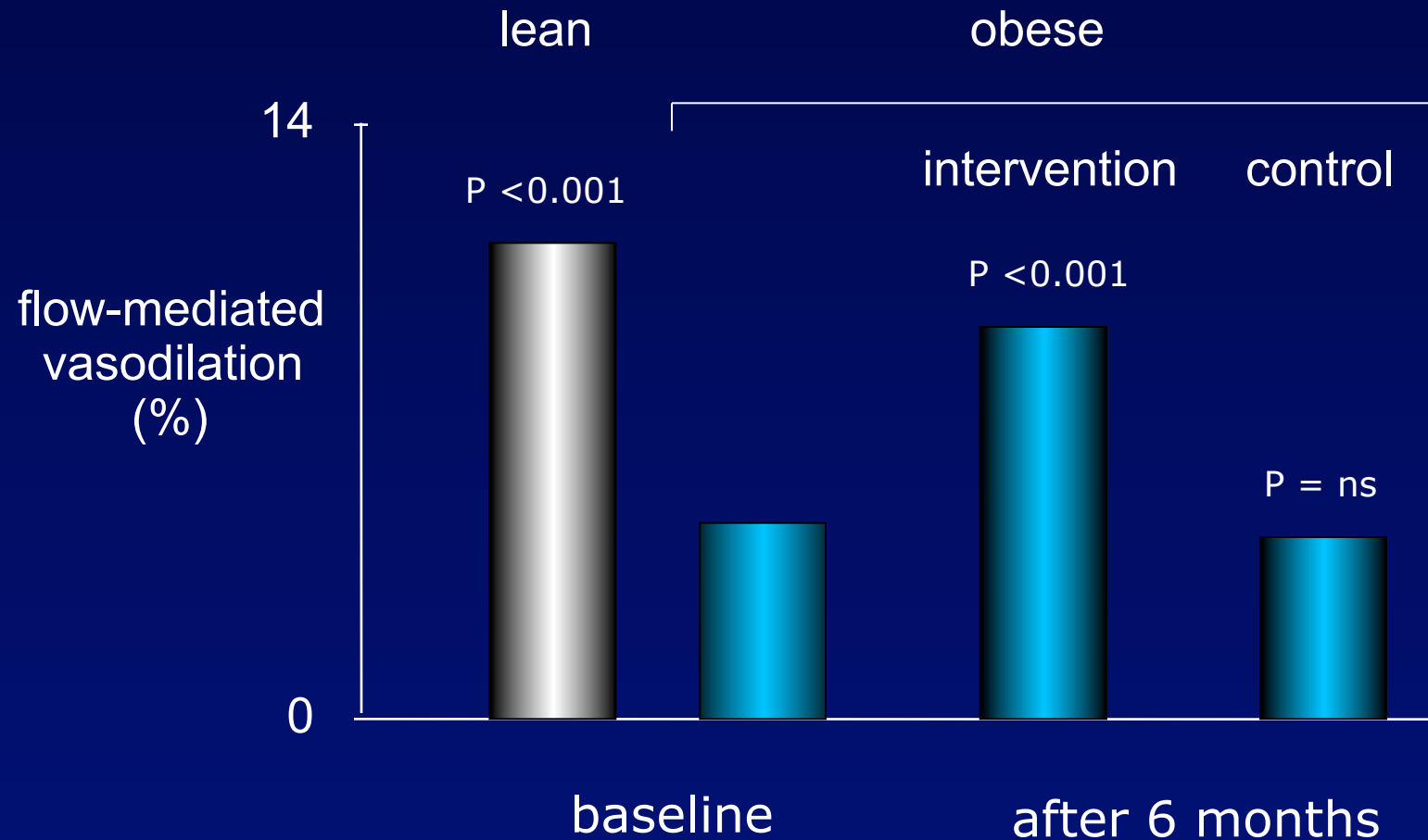
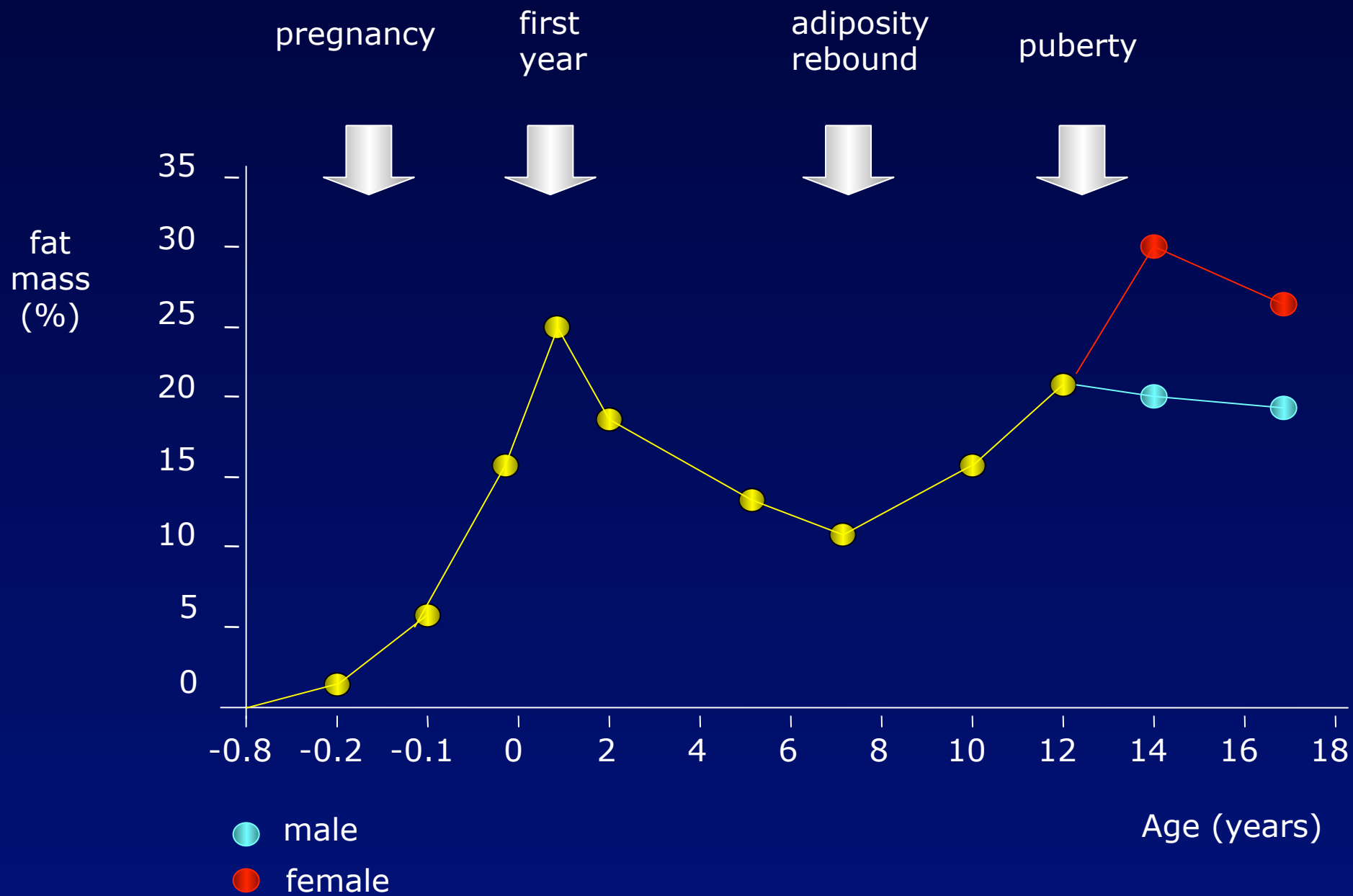
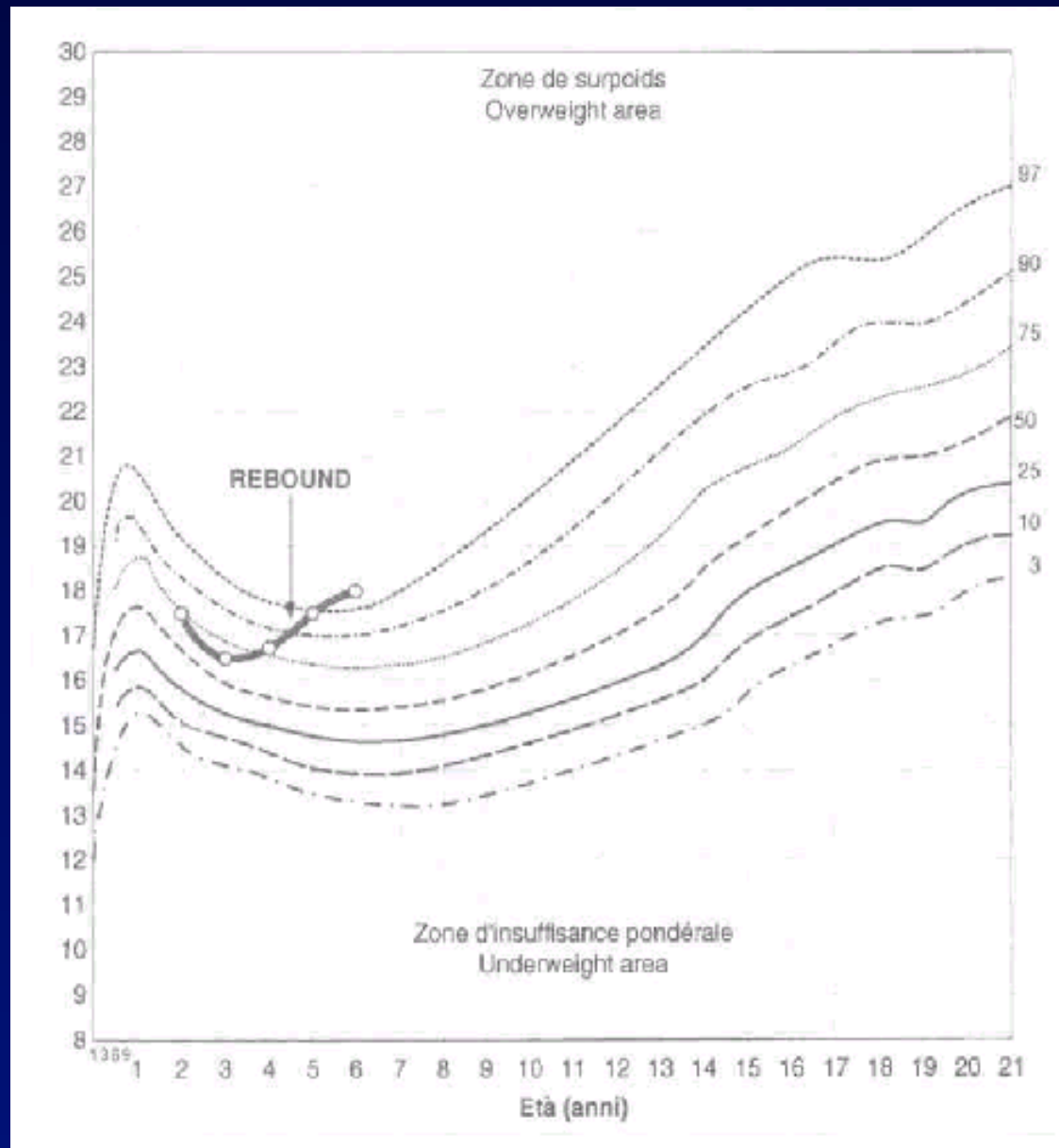
energy expenditure during walking and running in obese and nonobese prepubertal children

esercizio fisico nel bambino obeso

BMI (centile)	85°- 95°	95°- 97°	>97°
esercizio aerobico	anche con sollevamento del peso	preferibilmente senza sollevamento del peso	non sollevamento del peso
tipo di esercizio	brisk walking nuoto ciclismo aerobica sport di squadra danza sci pattinaggio tennis arti marziali	cammino nuoto ciclismo aerobica esercizi di forza e aerobici per le braccia e in scarico gravitazionale	nuoto ciclismo aerobica esercizi di forza e aerobici per le braccia e in scarico gravitazionale

effect of physical activity intervention on body composition in 425 6- to-10-year-old children

Intervention: PA after class, twice a week for 1 h, over 6 months

improvement of early vascular changes and cardiovascular risk factors in obese children after a 6-month exercise program

Meyer AA *et al.* J Am Coll Card 2007

pregnancy
first year
adiposity rebound
puberty
fat mass (%)
35
30
25
20
15
10
5
0
-0.8
-0.2
-0.1
0
2
4
6
8
10
12
14
16
18
male
female
Age (years)
Dietz WH Am J Clin Nutr 1994

adiposity rebound

LABORATORIO

glicemia (v.n. < 100 mg/dl: IGT: 100- 125; D > 126)

insulinemia (digiuno: v.n. < 15 mU/ml o gl/ins < 7)

colesterolo totale (v.n. < 180 mg/dl)

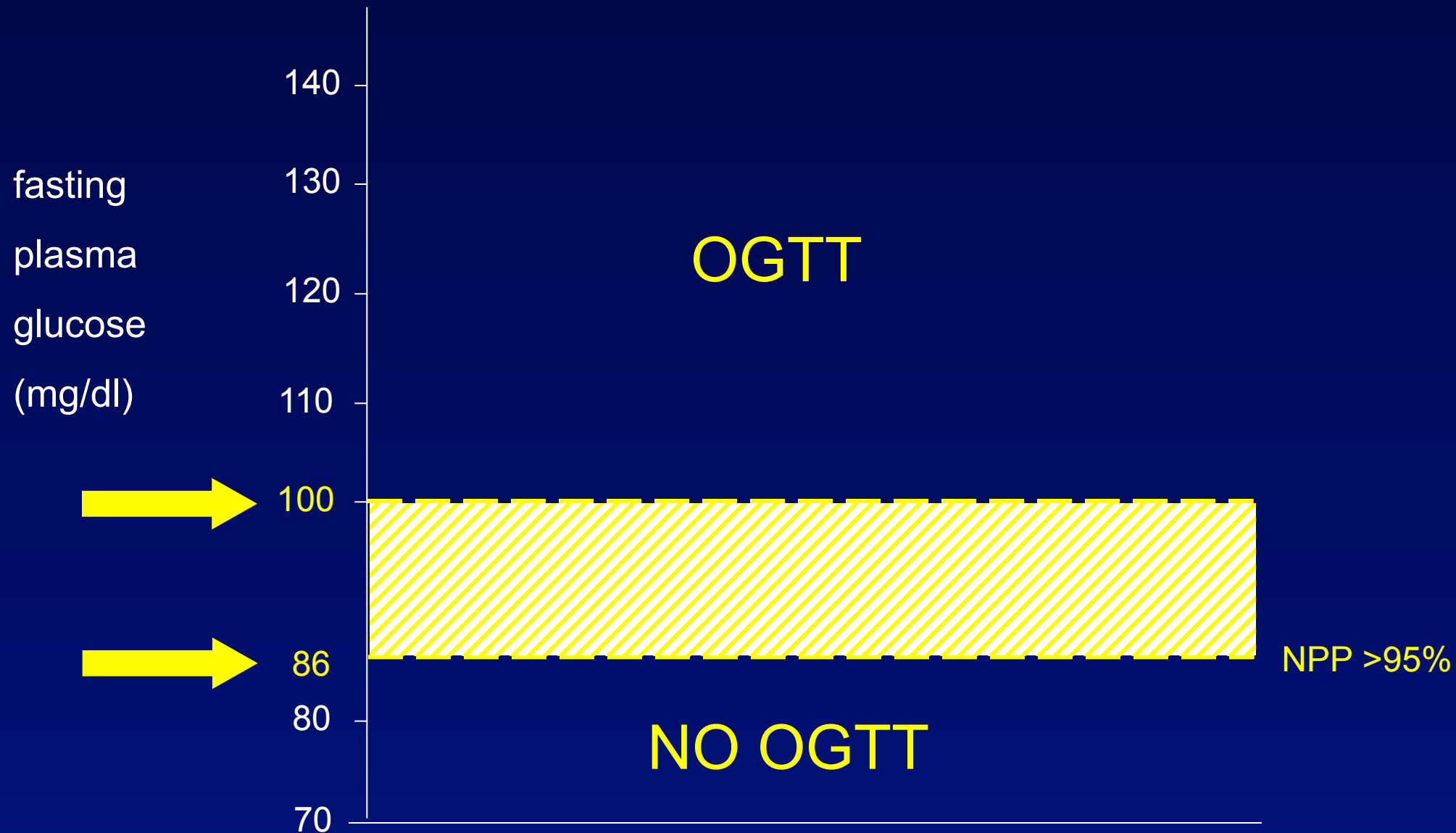
HDL (v.n. > 40 mg/dl)

LDL (v.n. < 130 mg/dl)

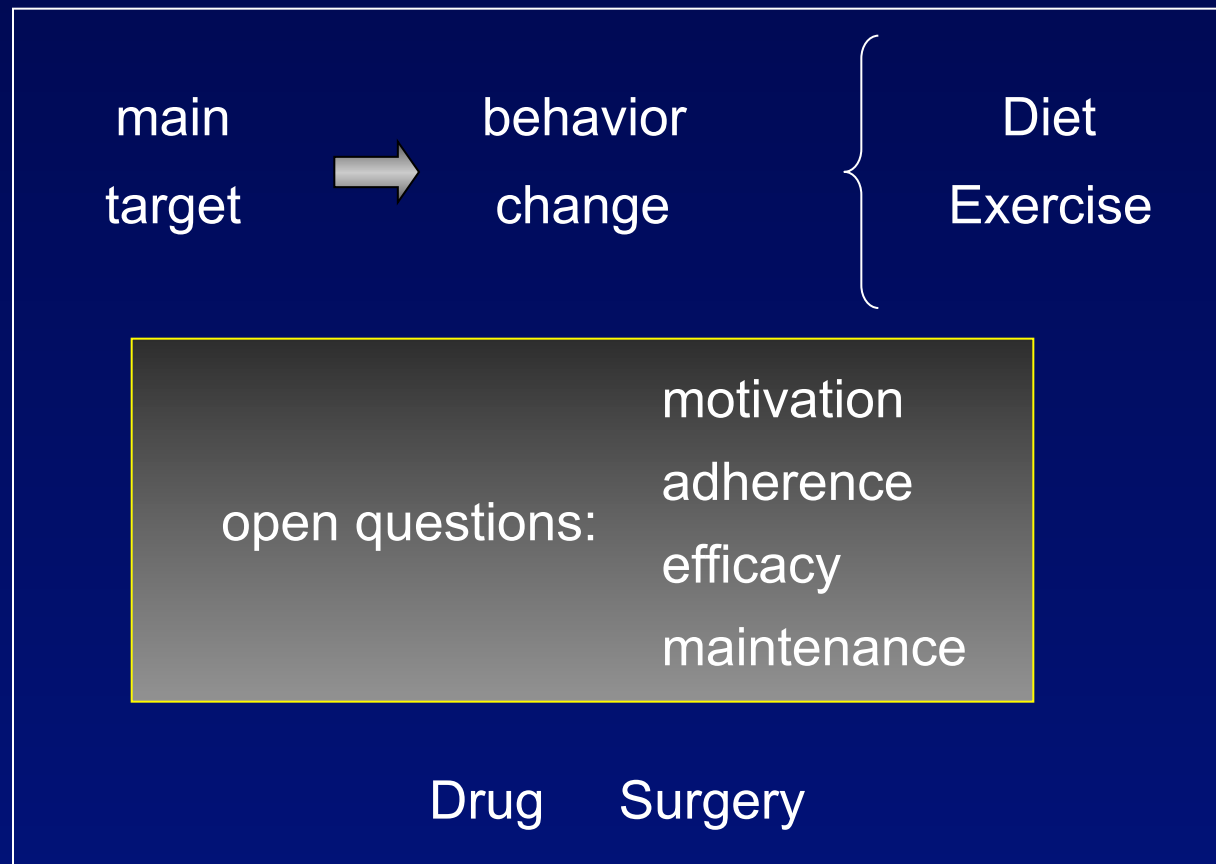
trigliceridi (95° centile, mg/dl)	maschi	femmine
0-4 anni	99	112
5-9	101	105
10-14	125	131
15-19	148	124

ALT (v.n. < 40 U/L)

fasting plasma glucose and impaired glucose tolerance in obese children

Maffeis *et al* Obesity 2009

therapy of obesity in children and adolescents

≤ 6 years	weight maintenence	(weight loss if weight-related complications)
> 6 years	weight loss	

Dietz & Robinson NEJM 2005

Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight & Obesity: Summary Report

Barlow SE & the Expert Committee Pediatrics 2007 (suppl.) (modified)

Target behaviors

Breastfeeding

Breakfast

Family meals (fast food)

Balanced macronutrients diet (RDA)

Fruits and vegetables, Fiber

Energy density

Portion size

Sugar-sweetened beverages

(Calcium)

TV other screen exposition

Physical activity